

COGNITIVE CONTROL OF ABSTRACT TASK RULES

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Abstract

Humans can perform complex behavior according to the goal of the task and its rules, and swiftly adapt their behavior to the new rule when there is a change in circumstances. How do our brains select and implement the appropriate rules? Cognitive control is the ability to select task-relevant information over other irrelevant distracting information. The neural mechanism of cognitive control is typically described in terms of resolution of conflict among sensory representations of stimuli or among competing motor responses. However, an understanding of the mechanisms by which the brain executes control over abstract, learned, representations of rule information has remained elusive. Moreover, it is unclear whether a single control mechanism governs different sources of conflict among task rules or whether dissociable mechanisms of cognitive control exist. In this dissertation, we used functional neuroimaging and behavioral experiments to examine the conflict-driven cognitive control mechanisms in humans for resolving conflict among abstract representations of task rules. By using a newly devised paradigm that can directly manipulate the degree of conflict at the task-rule level, we found conflict among abstract representations of task rules was resolved by feedback from the right inferior frontal gyrus enhancing the activity of the brain region processing the relevant abstract information, rather than suppressing the activity of the brain region processing the irrelevant abstract information. To examine the generality of the conflict-driven cognitive control mechanism, we independently manipulated the

levels of conflict for task switching (switch/repeat) and cue congruency (incongruent/congruent) using a factorial design. We found these two sources of task-rule conflict recruit different brain circuits for conflict resolution. Furthermore, by employing a behavioral proportion manipulation (changing the frequency of conflict trials within a single block), we found these two sources of rule-related conflict respond differently to the same manipulation. These results support a conflict-specific cognitive control account in which qualitatively distinct mechanisms recruit separate neural resources to resolve each type of conflict independently. Together, these findings provide a mechanistic view of how cognitive control of abstract rule representations is accomplished.

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1. Chapter 1: Selection of Task-relevant Information

1.1. Background and Significance

A hallmark of human cognitive faculty is the capacity for cognitive control: the ability to flexibly guide our thoughts and behavior in accordance with internally generated goals or task rules. This ability is particularly important when features of our environment simultaneously activate multiple, competing representations. Resolution of such conflict is thought to depend on cognitive control mechanisms, which bias information processing towards task-relevant representations over irrelevant competitors (Norman and Shallice, 1986; Desimone and Duncan, 1995; Miller and Cohen, 2001).

The mechanism involved in enhancing the task-relevant information at the expense of the task-irrelevant information is often referred to as “selection”. Selection mechanisms have typically been described in the context of selecting relevant over irrelevant sensory information from our external world, such as searching for a target object among other distractors in the scene. A consistent finding from both neurophysiological and neuroimaging studies is that activity increases in the brain areas encoding the task-relevant stimulus (Moran and Desimone, 1985; Corbetta et al., 1991; Wojciulik et al., 1998). Transcranial magnetic stimulation on prefrontal cortex in healthy human participants as well as studies on patients with focal prefrontal cortex damage also provide causal evidence that the source of the attentional modulation is likely from the prefrontal

cortex (Barcelo et al., 2000; Ruff et al., 2006; Taylor et al., 2007; Miller et al., 2011).

More recently, researchers have attempted to study the mechanism for selection of learned, abstract information. Some examples of this type of selection are, goal-directed retrieval of semantic or phonological features of a word (Gold and Buckner, 2002), and resolving conflicting conceptual representations (Badre and Wagner, 2007; Snyder et al., 2007). These studies often show that activation of prefrontal cortex is linked to selection of relevant conceptual knowledge from a set of competing alternatives, and that prefrontal cortex co-activates with dissociable posterior regions depending on the kind of information being retrieved. The similar neural pattern of activation for selection of perceptual (i.e. sensory) information and for selection of conceptual (i.e. abstract) information suggests a common selection mechanism underlying these two different types of information.

Here, we are interested in the selection mechanism involved in another type of learned abstract representation - task rules. We define “rule” as the if-then function that establishes relationships among a set of stimuli and potential responses, where such relationships are independent of particular stimuli or specific motor responses involved in the task. More specifically, the rules discussed here are abstract in a sense that they can be applied to familiar and novel situations alike (e.g. social rules), rather than being bounded by automatic or overlearned association between a stimulus and a response (e.g. a “red” light means to “stop”).

In recent years, several studies have indirectly tested the mechanism by which competing task rules were resolved by measuring changes of activity in brain areas that are selective for a particular task set (e.g. fusiform face area for gender discrimination task) under conditions in which task rules are constantly shifting (Yeung et al., 2006) or task performance requires conflict resolution (Egner and Hirsch, 2005). However, a common problem among these studies is that conflict can occur at multiple levels of information processing, ranging from perceptual inputs, motor response, to task rules. For example, in a typical task-switching paradigm, a task switch not only requires selection of new task rule, but also selection of the relevant stimulus features and appropriate responses specified by the currently relevant rule. Same problem also applies to tasks requiring conflict resolution such as the Stroop task. In order to successfully perform a Stroop color-naming task that involves a conflicting stimulus (e.g. the word GREEN displayed in red ink), participants need to enhance the relevant rule representation (color-naming task) and use it to select the relevant stimulus attribute (the color feature of the displayed word), and at the same time to resolve a pre-potent response tendency of reading the written word. Thus, without being able to separate rule representations from stimulus features and stimulus-response associations, it remains unclear how selection among competing “pure” rule representations is achieved and whether there is a common mechanism for selection among competing sensory representations (e.g. perceptual stimuli) and selection among competing abstract representations (e.g. task rules).

The overarching goal of this dissertation is to use functional neuroimaging to illuminate the cognitive control mechanisms for resolving conflict between task rules. Specifically, we want to investigate conflict resolution at the task-rule level, rather than having it confounded with other aspects of the task, such as the sensory properties of the cues or motor response.

A line of research has shown that neurons in prefrontal cortex can represent abstract rules that are not tied to specific stimuli or responses (White and Wise, 1999; Wallis et al., 2001; Bunge et al., 2003). In addition, the task rule representations in the prefrontal cortex are thought to provide the necessary top-down signals to bias processing in other brain structures towards the task-relevant information (Miller and Cohen, 2001). Despite mounting empirical evidence supporting the theory that conflicts occurring in the perceptual, memory, and motor domains are resolved through prefrontal bias in favor of the behaviorally relevant information over other competitors, very little is yet known about how competition among task rules themselves are resolved.

Answering the question regarding the selection mechanism of abstract rules would provide a basis for understanding higher-level cognitive processes that require selection of context-appropriate rules, such as planning, decision-making, problem-solving, and reasoning.

1.2. Literature Review: Selection from Concrete Sensory Representations

In what follows, I first review relevant theoretical perspective and empirical work in the field of visual selective attention that might inform our understanding regarding selection of competing abstract, non-sensory, representations. A central theme of this review will focus on the idea of biased competition. I will present numerous neuroimaging and neurophysiological studies that implicate prefrontal cortex as playing a critical role in selection of task-relevant information, and how this selection process can be achieved. Then, I will review relevant literature regarding rule selection, many of which are based upon task switching, a widely used paradigm that studies the cognitive processes involved in retrieval and/or selection of a currently relevant rule and resolution of task conflicts. A major goal of the current study is to examine the selection mechanism involved in resolving rule conflicts while controlling for other aspects of the task, such as the perceptual items and/or response sets associated with the rule representations.

1.2.1. Biased Competition: Attention, Working Memory, and Prefrontal Cortex

The visual system is limited in its capacity to process all visual inputs received at the same time. Therefore, selection mechanisms are needed to direct limited processing resources to the goal-relevant aspects of our surroundings. Several models have been proposed to account for how this attentional selection is achieved in the visual system. One classic view is that attention works as a mental spotlight, which enhances the responses of neurons

representing the behaviorally relevant stimulus in the visual field (Brefczynski and DeYoe, 1999). An alternative model, termed “biased competition model” (Desimone and Duncan, 1995), states that attention acts as a biasing signal that modulates the competitive interactions among neurons representing all of the stimuli in the visual field. Hence, the attentional enhancement of neurons representing the behaviorally relevant stimuli results in the suppression of other neurons representing the irrelevant stimuli. In addition, these competitive interactions can be biased through both “top-down” and “bottom-up” mechanisms (For a review, see Desimone, 1998). The “top-down” mechanism refers to the voluntary selection of stimulus that in accordance with our current goals or intentions (e.g. a stimulus is selected for its relevance to the current task requirement), whereas the bottom-up mechanism refers to the selection of stimulus given its salience (e.g. local inhomogeneity, sudden target onset, or novelty).

Some of the strongest evidence for the biased competition model in visual attention comes from the single-cell recording studies in monkeys using visual search tasks. In these studies, a pair of stimuli was presented simultaneously within the receptive field of a target neuron in visual cortex. When attention was not deployed to either stimulus, the neural response was shown to be a weighted average of the responses elicited by each stimulus alone, suggesting the stimuli within the receptive field appear to engage in suppressive interactions. When attention was deployed to one of the stimuli, the neural response was determined by the stimulus that the monkey attended to: the neuron gave a strong response

if the preferred stimulus for the neuron was attended, and the response was greatly suppressed if the non-preferred stimulus was attended (Moran and Desimone, 1985; Luck et al., 1997; Reynolds et al., 1999). This pattern of neural activity provides strong evidence that the neural responses are modulated by attentional selection.

Similar biasing effects that are found throughout visual cortex in visual search tasks also are found during the delay period of working memory tasks, in which the monkeys must hold the sample stimulus “on-line” for a couple of seconds in order to respond appropriately (Miller et al., 1993). The neural response of an inferotemporal neuron during the delay period in the matching-to-sample working memory task is biased to the behaviorally relevant choice stimulus: the neuron gives a strong response during the delay period followed by a preferred sample stimulus, but the response is suppressed followed by a non-preferred sample stimulus (Fuster and Jervey, 1981; Miyashita and Chang, 1988; Miller and Desimone, 1994). This similarity of biasing effects on neural activity in posterior sensory cortices suggests that selective attention and working memory share a common mechanism: neural activity is enhanced in populations of neurons representing behaviorally relevant visual stimuli, and inhibition occurs in populations of neurons representing competing stimuli by virtue of the mutually inhibitory interactions.

It is commonly believed that such biasing effect on neural activity is not an intrinsic property of the visual cortex, but rather is derived from interactions between brain regions or even between neural networks. It has been proposed

that the prefrontal cortex – the anterior portion of the frontal lobe that is highly developed in humans and primates – plays an important role in this process (Miller, 1999; Boller and Grafman, 2002). In terms of anatomy, the prefrontal cortex has extensive reciprocal connections with virtually all sensory and motor systems and a wide range of subcortical structures (Barbas and Pandya, 1989; Cavada and Goldman-Rakic, 1989; Petrides and Pandya, 2002), which makes it an ideal infrastructure for receiving diverse types of information about our current environment and internal states. The PFC's extensive outputs also allow for top-down control by providing an excitatory signal that biases processing in different brain systems to represent task-relevant information.

Both neurophysiological studies in monkeys and neuroimaging studies in humans also support the role of prefrontal cortex in exerting top-down control. Cooling studies in monkeys have shown prefrontal deactivation causes IT neurons during both the encoding and the delay period to be less selective. Furthermore, prefrontal cooling was accompanied by impairment in working memory performance, which established a direct link between prefrontal cortex top-down modulation and behavioral performance (Fuster et al., 1985). Similarly, microstimulation of neurons in the frontal eye fields have provided causal evidence that frontal cortex modulates neuronal activity in the visual cortex (Moore and Armstrong, 2003). In humans, studies in patients with prefrontal lesions as well as studies using transcranial magnetic stimulation of frontal regions also provide causal evidence of prefrontal-dependent top-down modulation on visual cortex (Barcelo et al., 2000; Zanto et al., 2011; Lee and

D'Esposito, 2012). Taken together, these findings provide neural evidence that the prefrontal cortex interacts with posterior sensory cortices to subserve working memory and selective attention. However, the question of *how* the prefrontal cortex influences processes in other parts of the brain is left unanswered. In other words, what is the nature of prefrontal cortex representations that enables the modulation of neural activity in other brain areas? The following section of literature review will focus on the role of prefrontal cortex in cognitive control, addressing the mechanism by which prefrontal cortex exerts control over other neocortical brain regions.

1.2.2. Prefrontal Cortex, Rule, and Cognitive Control

Cognitive control is the ability to flexibly adjust thoughts and behaviors to meet the current task requirement, by biasing processing in favor of task-relevant information over other more pre-potent competitors. Loss of cognitive control is marked by an overdependence on salient sensory cues or strong stimulus-response associations to guide behaviors. Such pattern of behavior is captured by humans with prefrontal damage (e.g. utilization behavior) and by monkeys with experimentally induced prefrontal lesions (e.g., Bianchi, 1922), suggesting prefrontal cortex – a neocortical region that finds its greatest elaboration in humans, is centrally involved in cognitive control. The previous section summarized a line of studies that implicate prefrontal cortex as the source of top-down control that biases processing in other parts of the brain towards task-relevant information. Here, I will review several theories regarding the

mechanisms by which prefrontal top-down control is achieved, and how the prefrontal control process is regulated, so as to provide a comprehensive mechanist view for cognitive control.

1.2.2.1. Miller and Cohen's Integrative Theory of Cognitive Control

What is the nature of prefrontal cortex representations that enables the modulation of neural activity in other brain systems for attention (sensory systems), recall (memory system), and response selection (motor system)? One prominent theory of cognitive control proposed by Miller and Cohen (2001) states that prefrontal cortex exerts control over other brain areas by representing and maintaining of a specific type of information in working memory – the goal or the rule information. Specifically, the rule representations in the prefrontal cortex are like “maps”, which configure the neural pathways within and between other brain areas that are needed to perform the task. In other words, rule representations maintained in the prefrontal cortex provide a mechanism of top-down control by guiding the flow of neural activity along the task-relevant neural pathways, thereby establishing appropriate mappings between sensory inputs, internal states, and outputs needed to perform a given task. Thus, from this perspective, biased competition serves as a general mechanism by which different types of representations (e.g. perception, memory, or response) are processed by the brain.

The majority of empirical support for rule information maintained via the prefrontal cortex stems from single-cell recording of monkey's prefrontal cortex during working memory tasks. Neurophysiological studies have shown that the prefrontal neurons are highly sensitive to abstract rule information: as many as 30% to 40% of randomly selected prefrontal neurons respond to task rule after training (Asaad et al., 2000; Wallis et al., 2001; Bunge et al., 2003), which sometimes outnumber prefrontal neurons encoding sensory information (Cromer et al., 2010; Roy et al., 2010). In addition, prefrontal neurons appear to be highly adaptive and can represent multiple, independent, categories based on task demands (Cromer et al., 2010). This high adaptability and representational power of prefrontal cortex may underlie its ability to engage a variety of complex tasks with limited number of neurons. There is also some neural evidence from human neuroimaging studies show populations of neurons in prefrontal cortex can encode abstract rule information (Haynes et al., 2007; Montojo and Courtney, 2008). Taken together, these findings support Miller and Cohen (2001) that the prefrontal cortex subserves cognitive control by actively maintaining and representing rule information.

1.2.2.2. Botvinick's Conflict Monitoring Model

One central question for theories of cognitive control is how the system determines when control is required. In Miller and Cohen's theory of cognitive control (2001) and a number of others (Norman and Shallice, 1986; Baddeley and Della Sala, 1996), none have offered an account of how the need for control

is detected. The lack of such an account renders the notion of cognitive control again at the hand of a homunculus. To address this problem, Botvinick and colleagues proposed a conflict-monitoring model that specifies a system that monitors for the occurrence of conflicts in information processing. Once this “conflict monitoring” system detects conflicts (presence of simultaneous activation of competing representations), it passes on this information to the control system, which exerts control by biasing information processing towards task-relevant information to resolve conflicts. This model also suggests the anterior cingulate cortex serves as the conflict-monitor system and the lateral prefrontal cortex serves as the strategic-control system, providing a self-regulating neural circuit for cognitive control. Initial evidence supporting the conflict-monitoring model comes from studies showing the so-called “conflict adaptation effect” - the ramped up of control following a conflict event. For example, Gratton et al. (1992) showed that the level of interference from a task-irrelevant stimulus (“conflict”) is reduced following incompatible trials in the flanker task. That is, participants respond faster and more accurate in an incompatible trial if it was preceded by another incompatible trial (il) compared to a compatible trial (cl). Similar behavioral effects were also found in the Stroop task (Sturmer et al., 2002) and Simon task (Jones et al., 2002). Other convincing evidence comes from human neuroimaging studies. Using the Stroop color-naming task, Kerns et al. (2004) showed greater ACC activity on the previous incongruent trial predicts better behavioral adjustment (faster RT) and greater

prefrontal cortex activity on the current incongruent trial, supporting a role of anterior cingulate cortex engaged in conflict monitoring.

Later developments of this theory have focused on whether the self-regulating conflict-control circuit proposed in the original model operates in a “domain-general” or “domain-specific” manner. Several studies have utilized the “conflict adaptation effect” described above to test whether the control process recruited by one type of conflict (e.g. Stroop conflict) can facilitate the resolution of another type of conflict (e.g. Simon conflict) (Kunde, 2003; Wendt et al., 2006; Egner, 2007). If the up-regulation triggered by one type of conflict were to facilitate the resolution of another type of conflict, then it would support a domain-general model of conflict adaptation. Otherwise, it would support a domain-specific model of conflict adaptation. Overall, results from these studies are more in line with the “domain-specific” hypothesis of conflict resolution, as conflict types are found to be non-interactive (for a review, see Egner, 2008). This “domain-specific” hypothesis has interesting implications in the way we think about “control”. If conflict resolution were indeed conflict-specific, there might be dissociable and specialized conflict-control circuits that can operate in parallel to detect and resolve conflicts arising from different types of representations (e.g. stimulus-stimulus conflict, stimulus-response conflict). In relation to our hypothesis, it is even possible that a different neural circuit will be recruited for conflict resolution of rule representations that is independent from those recruited for response conflicts.

Finally, it is worth noting that a self-regulating conflict-driven control system is more closely in line with what's known as "reactive control". That is, the control is triggered automatically by an internal signal of uncertainty. This control process operates differently from the goal-directed "proactive control", such as actively maintaining the goals or task rule information in mind to enable optimal cognitive performance, similar to what was proposed in Miller and Cohen (2001) integrative cognitive control model. In the following section, I will review Braver et al. (2007) dual mechanisms of control framework to further examine the two distinct control processes.

1.2.2.3. Braver's Proactive and Reactive Control Modes

From this framework, there are two qualitatively distinct control modes for resolving conflicts: "proactive control" and "reactive control". In the proactive control mode, the goal-relevant representations are actively maintained in a preparatory manner until the successful completion of the task. On the other hand, in the reactive control mode, the goal-relevant representations are only retrieved or re-activated after a high interference event is detected. This model supports a view that different cognitive control mechanisms need not engage through anatomically distinct brain regions, but rather be implemented at different points in time. Specifically, proactive control is associated with sustained activity occurring at the time when contextual cues are presented (cued-based), whereas the reactive control is associated with transient activity triggering by the incongruent probe (probe-based).

Burgess and Braver (2010) demonstrated the temporal dynamics of prefrontal cortex activation changes as a function of task demands using a recent-probes item-recognition task. In this study, they manipulated task demands by varying the frequency of recent negative probes (a non-target probe appeared as target in the previous trial) in a block. During the high interference expectancy blocks (frequent recent negatives), the activity in left lateral prefrontal cortex increased during the delay period and lasted for the entire block, consistent with recruitment of proactive control. On the contrary, in the low interference expectancy blocks (rare recent negatives), the activity in left inferior prefrontal cortex (a slightly different prefrontal area) exhibited a transient increase of activity at the time of the probe, specifically during the recent negative probe trials, consistent with the recruitment of a reactive control.

There are several interesting points we can take away from this dual control model. First, control processes can operate through multiple routes towards successful task performance. For one, control may be drawn upon to emphasize the task-relevant features such that it preempts the irrelevant distractors from entering working memory, as in the case of proactive control. Alternatively, when both relevant target and irrelevant distractors enter working memory and compete for cortical representation, control may excite only the stimulus-response mapping for the relevant stimulus and/or suppress the stimulus-response mapping for the irrelevant stimulus, as in the case of reactive control. In addition, task demands may be the determining factor when weighing between proactive and reactive control strategies. Therefore, it is possible that

small changes in an otherwise similar task might lead participants to resort to a different strategy, resulting in different activation pattern.

1.2.3. Summary

The biased competition model of visual attention suggests that the neural activity in visual cortex is modulated by the effect of attention on an underlying suppressive interaction among competing stimuli, where neural activity is enhanced in neurons coding the behaviorally relevant visual stimuli at the expense of the neurons coding the irrelevant stimuli. Several lines of evidence suggest that the prefrontal cortex provides the top-down influence to bias information processing in the posterior cortices. It is thought the prefrontal cortex exerts control over other brain areas by sustained active maintenance of goals or task rules in working memory, to bias attention, memory, and action systems in a goal-driven manner. To answer the question concerning how control systems “know” when to exert top-down control to bias processing, a conflict-monitoring component is proposed in which ACC detects occurrence of conflicts in information processing, thereby triggering compensatory adjustments in prefrontal control. Finally, cognitive control can operate at different point in time, or speaking in a broader context, control processes can operate through multiple routes: it can either operate proactively, as in the anticipatory maintenance of goal-relevant information before its implementation. Alternatively, it can proceed reactively, in which both irrelevant and relevant representations associated with the target were retrieved, and control proceeds to select the appropriate one.

While these models provide valuable insights in terms of how cognitive control might be implemented by the prefrontal cortex, what remains unclear is the precise nature of the type of information prefrontal cortex represents, which allows it to modulate activity in other parts of the brain. According to the cognitive control theory by Miller and Cohen (2001), the prefrontal cortex exerts control over other parts of the brain by maintaining abstract rules or goal information in working memory. Thus, in what follows, I will review a line of literature regarding how abstract rules are represented, maintained, and implemented by the brain, so as to get a better understanding of what role do task rule representations play in cognitive control.

1.3. Selection from Abstract Rule Representations

Much of our daily behavior is guided by task rules. While some rules are based on well-learned stimulus-response associations (e.g. see a red light, put on the brake), others are more abstract in a sense they are not tied to specific sensory stimulus responses and can be applied to situations alike. For example, we can apply what we learned about dining etiquettes from restaurants visited in the past to a brand new restaurant. This ability to represent “abstract rule” is thought to critically depend on prefrontal cortex, because damage to this area often leads to deficits in the patient’s ability to perform tasks requiring higher orders of abstraction, while sparing the ability to perform lower-level, simple contingency tasks (Badre et al., 2009).

When studying how do neurons in prefrontal cortex represent abstract rules, many neurophysiological and human neuroimaging studies in the past have used rules that are tied to specific stimulus features (e.g. location-matching rule vs. shape-matching rule as in the study by Hoshi et al., 2000) or behavioral responses (e.g. fixed stimulus-response associations as in Murray et al., 2000; Passingham et al., 2000). Such studies can be problematic when it comes to the interpretation of rule-specific activity in prefrontal cortex, because the difference in the distribution of neural activity revealed by comparing one rule versus another may simply reflect attention to the sensory properties of the cue that the subjects were required to maintain in working memory (e.g. the specific location or shape information of the cue) or reflect the preparation of specific motor response that was automatically triggered by the cue stimulus, rather than the task rules themselves (e.g. location-matching rule: *if* the location of the cue matches to the target item, *then* press left key).

More recently, several investigators, including those in our lab, have attempted to address this problem by studying abstract rules or relational information that are independent from specific sensory features or behavioral responses (Montejo and Courtney, 2008; Ackerman and Courtney, 2012; Ikkai et al., 2014). So far, these studies support the view that different brain networks represent non-sensory abstract information and sensory-specific item information.

Thus, in the following section, I will review the neural representation of abstract rules, addressing the critical role of prefrontal cortex in representing and

maintaining rule-specific information that serves to bias information processing in other brain areas. Particularly, the “abstract” rules are defined as general rules or principles that are not tied to specific events (sensory features or behavioral responses), and can be extended to situations alike. Then, I will discuss the cognitive control processes associated with abstract rule use. For example, the control process associated with shifting between task rules (e.g. task-switching) and resolving conflicting task rules (e.g. Stroop). This would allow us to get a better understanding of the neural mechanism involve in the control of abstract representations, such as task rules.

1.3.1. Representation of Rules

Goal-directed behavior requires the ability of the brain to extract regularities across experiences of our interactions with the environment. By forming associations between contexts, actions and their outcomes, we can develop an internal representation of the “rule of the game” that allows us to make predictions of what actions are likely to achieve our current goal in a given context, and what to anticipate in similar situations. Therefore, the representation of a task rule might be encoded by neurons whose activity reflects the learned relationships between events. Neurons in prefrontal cortex do reflect such property: many of them develop selectivity for learned associations between sensory cues, voluntary actions and rewards (Watanabe, 1992; Asaad et al., 1998; Fuster et al., 2000). However, if each experience were to store as association between events, then it would require a prodigious amount of

storage. Luckily, our brains have evolved the ability to abstract rules or principles from specific experiences. The ability to represent abstract rules allows us to deal with different situations without needing to memorize every specific relationship between events. It also allows us to deal with novel situations. So how are abstract rules encoded in the brain? What is the neural correlate for representing abstract rule information?

Support for a role for prefrontal neurons in representing abstract rules comes from neurophysiological studies of monkeys alternated between different task rules (Hoshi et al., 1998; White and Wise, 1999; Asaad et al., 2000). For example, Hoshi et al. (1998) trained monkeys to reach a target that either matched the shape (shape-matching rule) or the location (location-matching rule) of the cue, the correct response depended on which rule was currently in effect. They found that some neurons in the prefrontal cortex were selective for the target features (circle vs. triangle), regardless of the task. On the other hand, they also found some neurons were selective for the type of task (shape-matching vs. location-matching task), despite it is the same target item. In other words, for the same target item, these neurons responded differently depending on the task rule. Such rule-selective prefrontal neurons have also been found in other studies utilizing different types of rules, such as “object” vs. “spatial” vs. “associative” rules (White and Wise, 1999; Asaad et al., 2000).

In all of these tasks described above, these rules are directly tied with particular sensory features of the cue; therefore, the difference in the distribution of neural activity revealed by comparing one rule versus another may simply

reflect attention to the sensory properties of the cue that the subjects were required to maintain in working memory (e.g. the specific location or shape information of the cue), rather than the task rules per se (e.g. location-matching rule: *if* the location of the cue matches to the target item, *then* press left key). The rule-specific activity should be independent from any specific stimulus features. This problem was addressed in a neurophysiological study (Wallis et al., 2001) using operation-specific rules, rather than domain-specific rules that are based on the sensory domain/feature of the cue. In this study, monkeys were trained to respond whether two successively presented pictures were identical or different. The “match” rule requires the release of a bar when two pictures match. On the contrary, the “non-match” rule requires the release of a bar when the two pictures don’t match. In addition, to disambiguate neural activity related to the sensory properties of the cue from the rule that the cues signified, the researchers used two distinct cues from different sensory modalities to signify the same rule. They found a group of neurons in prefrontal cortex were selectively active for one rule over the other. Moreover, monkeys were able to make correct responses for stimuli that they just saw for the first time, which further supports the hypothesis that neurons in prefrontal cortex have the capacity to represent abstract rules.

Bunge et al. (2003) used a task similar to that of Wallis et al. (2001) to study abstract rule maintenance and retrieval in humans. By including a delay period during which participants were required to either maintain the “match” or “non-match” rule or a simple stimulus-response relationship, the researchers

found frontal, parietal and temporal cortices were sensitive to rule type during cue presentation, suggesting that they were involved in rule retrieval. On the other hand, only the ventrolateral prefrontal cortex and parietal cortex continued to show sensitivity to rule type during delay period, suggesting that they were relatively more involved in maintenance of the relevant response contingency. However, another interpretation for the match vs. non-match tasks is that subjects learned the match rule as the default strategy; and to perform the non-match task, they simply perform the default match task and then reverse the button press response contingency. In that case, the observed brain activity may reflect preparation of motor response, rather than abstract rule representations (match rule vs. non-match rule).

In another study, Haynes et al. (2007) used multivoxel-pattern classification analysis (MVPA) to test whether the increased activity normally observed throughout prefrontal cortex during the delay period in working memory tasks actually contains rule-specific information (i.e. signals related to rule preparation). Participants in this study freely chose between two arithmetic operations (subtraction vs. addition) and performed a calculation based on two random numbers. The researchers found the spatial pattern of BOLD signals in the anterior region of medial prefrontal cortex successfully predicted which of the two tasks the participants were intending to perform. Since the arithmetic operations are not tied to any specific sensory stimuli or responses, this study provides strong evidence that abstract rules can be represented by distributed patterns of activity in the prefrontal cortex.

So far, the above studies suggest that neurons in the prefrontal cortex can represent and maintain abstract rule information that is independent from any physical attributes. But how do these abstract rule representations interact with or influence on one another in order to guide behavior? For example, when a stimulus invokes a set of rules, how should we choose? Or consider a situation where one needs to flexibly switch between different rules to meet the changing environmental demands. How is the shifting between task rules achieved? In the previous section, I review a line of work regarding the cognitive control mechanisms for concrete (sensory) information. When two sensory stimuli within a cell's receptive field compete for cortical representation, the competition is resolved by enhancing activity in the brain area representing the task-relevant stimulus at the expense of the brain area representing task-irrelevant stimulus. Can similar mechanism also apply to abstract rule representations? In what follows, I will discuss the cognitive control processes associated with abstract rules using task-switching paradigm. In this paradigm, participants are required to switch between two competing tasks (or, strictly speaking, to switch between appropriate rules of a task). An understanding of the cognitive control mechanisms for task switching would allow us to answer questions such as how selection between abstract rule representations is achieved.

1.3.2. Task Switching

Task switching paradigm is frequently used to study how are appropriate task sets selected and implemented according to new task requirements. A "task

set” typically refers to the rule of a particular task, whose representation is independent from other sensory aspects of a task, such as task cues and task targets (Sakai, 2008).

It is typically observed that task performance is slower and less accurate when switching between two tasks compared to repeating the same task in sequence (Jersild, 1927; Logan and Bundesen, 2003; Monsell, 2003). The additional time needed for task switching compared to task repetition is referred to as “switch cost”, which is thought to involve cognitive control processes necessary for updating task goals and/or setting up for the new task set (for a review, see Sakai, 2008).

There are two main theories that provide different explanations with regards to the source of switch costs: (1) the task-set reconfiguration hypothesis (TSR; Rogers R.D., 1995; Brown and Besner, 2001); and (2) the task-set inertia hypothesis (TSI; Allport et al., 1994).

The TSR hypothesis suggested that switch costs reflect the time needed to reconfigure the cognitive system for the upcoming task set. In order to perform a task, participants enter a task-dependent cognitive state, and this state will remain constant throughout the duration of the task until another task state is required, at which time control processes shifts the system into a new task state (Logan and Gordon, 2001). From this perspective, TSR may involve inhibition of the previous task set as well as activation of the new task-set. This theory also predicts that if sufficient time is allowed to prepare for the upcoming task, the switch costs should be eliminated. In support of the TSR account, it was found

that lengthening the interval between task cue and stimulus onset (i.e. preparation time) significantly reduced the observed switch costs (Meiran, 1996; Meiran et al., 2000). However, this preparation benefit reached a substantial asymptote after ~600 ms of preparation (Monsell, 2003). One possible explanation is that task set reconfiguration processes cannot be done until the stimulus attributes exogenously triggers the associated new task set (Rogers R.D., 1995). This exogenous task switching process is thought to be independent from the endogenous control process that emphasizes the deliberate intentions that are governed by goals.

On the other hand, the task-set inertia hypothesis proposed that switch costs are the result of proactive interference from the previously performed task. This hypothesis was supported by a variant of the Stroop task in which participants switched between the less practiced color-naming task (a “weaker” task set) and the more practiced word-reading task (a “stronger” task set). Asymmetric switch costs were observed in the study – the switch costs were significantly greater when switching to the more familiar word-reading task set compared to switching to the less-practiced color-naming task set (Allport et al., 1994). The asymmetry of switch costs cannot be explained by the task set reconfiguration hypothesis, because reconfiguration to a more familiar, and hence stronger task set, should take less time for the brain system to reconfigure to the new task state. Rather, the TSI account (Allport et al., 1994) states that successful performance of the weaker task (color-naming) requires greater cognitive control resources to bias the relevant color-naming task pathway and to

inhibit the competing task representations from the stronger word-reading pathway. Consequently, this inhibition carries over to the next trial, which results in greater difficulty to retrieve these previously inhibited word-naming task representations. In addition, the compensatory enhancement of the weaker color-naming task also carries over to the subsequent trial and further interferes with access to the word-reading task set. Hence, according to task-set inertia account, switch costs reflect the extra time and effort to resolve competition from the previously activated task set.

Yeung et al. (2006) has provided support for the task set inertia hypothesis by using functional neuroimaging to investigate between-task competition in a task-switching paradigm. Specifically, participants in this study were presented with overlapping face and word stimuli and switched between a face task (judging the gender of the face) and a word task (judging whether the word has two syllables or not). Because word stimuli and face stimuli activate distinguishable cortical areas, this approach allows the researchers to measure the task-dependent neural activity when participants switched from one task to another. The researchers found that activity increased during a task switch in brain areas selective for the previous, now-irrelevant task, and that the behavioral switching cost positively correlated with the switch-related neural activity in the task-irrelevant areas (areas selective for the previously relevant but now irrelevant task), but not the task-relevant areas (areas selective for the currently relevant task). These results support the task-set inertia hypothesis

that interference from a recently performed task is a determining factor for switch costs.

Despite the proactive interference from the previously performed task is a well accepted theory for explaining switch costs, it is now more of a consensus among researchers that a part of the switch costs also reflects the time-consuming, endogenous, task set reconfiguration process (Monsell, 2003).

However, the foregoing accounts of how appropriate task sets are selected and implemented according to current task requirements is not without problem.

First, many of the task-switching paradigms that were used to study task selection required participants to select different levels of representations, ranging from selection of perceptual inputs (e.g. attending to the external cue or select relevant stimulus features), task rule representations (e.g. retrieving task rules from memory), to motor response (e.g. selecting appropriate response for a given stimulus). Thus, during a task switch, a combination of these processes needs to be internally reconfigured for successful performance. This is problematic because the task rule selection process is conceptually different from those involve response selection and perceptual selection. It remains unclear how selection of purely abstract rule representations is achieved and whether there is a common mechanism underlying the selection of different types of information (e.g. memories, perceptual stimuli, rules, responses). As previously discussed, both single-cell recording and human fMRI studies have shown prefrontal neurons can represent abstract rules. However, it remains unclear whether prefrontal cortex can also be the source of the bias signal for selection of

task rules that it represents. In other words, can the process of bias competition also take place within the prefrontal cortex? To answer this, the first logical step would be to design a new paradigm that can separate rule-based selection process from stimulus-based or response-based selection processes. This is addressed in Experiment 1 (Chapter 2) where we introduced an experimental manipulation that varied the degree of conflict in selecting task rules independently from the sensory features of the cue and cue-trigger behavior responses. We then investigated whether the source of top-down modulation that resolves competition between abstract rule representations is derived from structures within prefrontal cortex, and whether the principle of biased competition also applies to the selection of competing abstract information, such as selecting relevant over irrelevant task rules.

Second, there may be two different control processes involved in task switching: 1.) The endogenous (i.e. goal-driven) process that involves the activation of the new task rule according to the current goals or context, independent of specific stimuli and responses; and 2.) The exogenous (i.e. stimulus-driven) process that involves the activation of a task set invoked by the stimulus attributes. As mentioned earlier, lengthening the preparation time between cue and stimulus onset does not totally eliminate switch cost. The residual switch cost has been linked to exogenous processes that only come on-line at the time of target presentation (Rogers R.D., 1995). Thus, in order to more directly study the endogenous (goal-driven) process of how appropriate task sets are selected, one needs to design a new paradigm that emphasize the

voluntary selection process of the relevant task rule. That is, rather than having a task cue that is always associated with or automatically invokes the same task set, the participants need to know the current context in order to correctly retrieve the meaning of the task cue. This context-dependent task selection process is partially tested in a study by Brass and von Cramon (2004). The authors devised a new task-switching paradigm in which participants were required to alternate between a parity task, a number task, or no task at all; the instruction was based on a task cue preceding target items (number from 1 to 9, except 5). Importantly, the task cues had two different dimensions: color and form. The relevant dimension was indicated at the beginning of each block and alternated across blocks throughout the experiment. The relevant and irrelevant dimensions could either indicate the same task (congruent cue) or different tasks (incongruent cue), or no task at all (neutral cue). Because the bivalent cues (congruent and incongruent) did not always provide unequivocal task information, the selection of relevant task rule required maintenance of goals or relevant contexts (color or form) in working memory to bias task selection. Thus, successful performance relied heavily on the endogenous control of task selection. The authors were able to show greater activation in lateral prefrontal cortex and intraparietal sulcus when contrasting the bivalent conditions (congruent and incongruent) to the univalent condition (neutral). Because this selection process was specifically based on the processing of the cue, the observed activations suggested that these two areas were involved in the endogenous selection of relevant task context that in turn determines the appropriate task rule. However, to the

authors' surprise, the contrast between congruent condition and incongruent condition did not yield significant difference, neurally or behaviorally. The main reason for such null result is thought to relate to the weak association between cue dimensions and task rules. In their task, both relevant and irrelevant dimensions of the cue were only weakly associated with task rules. Therefore, it is very likely that the irrelevant dimension of the cue were not able to automatically elicit the retrieval of the associated task rule. To overcome this, it is assumed that a pre-test training procedure on the associations between cue dimensions and task rules is required. The training procedure would be incorporated into our own experimental design in order to successfully produce conflicts at the task rule level.

1.4. Conclusions and Open Questions

While much is known about the cognitive control mechanism associated with sensory information, relatively little is known about the cognitive control mechanism for abstract information such as task rules. For example, how conflict among abstract rule representations is resolved? How switching or shifting between abstract rule representations is achieved by the brain? Is the cognitive control mechanism for rule information conflict-specific or domain-general? Therefore, the main goal of this dissertation is to investigate various control processes associated with abstract rule representations.

In order to study the “pure” abstract rule representations independent from any stimulus features or behavioral responses, the current study utilized a new

paradigm in which we manipulated the degree of conflict directly at the task rule level. We defined abstract rule as the if-then function that establishes relationships among a set of stimuli and potential responses, where such relationships are independent of particular stimulus properties or motor responses that are associated with the stimulus.

Experiment 1 seeks to elucidate the cognitive control mechanisms responsible for resolving conflicts among abstract rules. Specifically, in order to select the appropriate task rule to correctly produce the desired behavior, the participants need to know the current context and use it to guide the selection of task rule. Thus, this allows us to more directly study the endogenous (goal-driven) process of task rule selection. The main hypothesis to be tested in this experiment was whether abstract rule representations can be maintained as a type of information in working memory via prefrontal cortex, and the process of biased competition occurs between the prefrontal cortex and sensory or motor regions also occurs within the prefrontal cortex itself, by biasing neural processing towards the prefrontal neurons coding the relevant abstract task rule over the irrelevant one. Alternatively, the selection mechanism responsible for resolving conflicts among abstract rules may be qualitatively different from those resolving conflicts among stimulus properties or motor responses. If that is the case, then other selection mechanisms will need to be proposed for resolving conflicting rules.

Experiment 2 in this dissertation is a direct follow-up to experiment 1 and uses the same paradigm and data set to ask the question that whether the

cognitive control mechanism for goal-driven rule selection different from that of stimulus-driven rule switching. As previously discussed in the task-switching section, part of the switching cost for shifting between rules reflects the stimulus-driven process which involves the activation of a task set invoked by the cue stimuli. In any given task-switching paradigm, each of the cue stimuli is always associated with the same task rule throughout the course of the experiment (e.g. triangle cue always means task A and circle cue always means task B). Therefore, after doing multiple trials, task performance becomes more stimulus-driven, as the meaning of the cue stays constant. In comparison to our current experimental design, participants are required to remember the context in which the cue was presented to correctly retrieve the meaning of the cue, and at the same time, to switch rules across trials. Therefore, the current experimental design allows us to examine the control processes associated with two different sources of task conflict: rule selection and rule switching. This allows us to answer the bigger question that whether the cognitive control mechanism recruited to resolve conflict between abstract rules is conflict-specific (dissociable cognitive control systems) or domain-general (single cognitive control system).

Cognitive control can be modulated by task demands. According to the conflict monitoring literature, congruency effects can be modulated by the proportions of incongruent trials versus congruent trials within a single block. In Experiment 3, we further investigate the specificity of cognitive control for resolving different types of task conflict (i.e. switch between different task rules versus selecting appropriate task rule over the inappropriate one) by introducing

a proportion conflict manipulation. Specifically, the goal was to see whether (1) the proportion manipulation would have similar effect of conflict resolution on both conflict types; and (2) whether the effect of proportion manipulation for one conflict type would transfer to the other conflict type within the same block. This would help to answer the question concerning the specificity of cognitive control mechanisms for resolving different types of conflict between abstract rules.

2. Chapter 2: Conflict Resolution of Abstract Rules

2.1. Introduction

Goal-directed behavior is thought to depend on the ability of the brain to represent and implement the task rules that would produce appropriate behavior for a given situation. Studies have shown that neurons in the prefrontal cortex (PFC) can encode abstract task rules that are not bounded by a specific set of stimuli or overlearned stimulus-response associations. Rather, these rule representations support generalization of task performance to familiar and novel situations alike (Asaad et al., 2000; Hoshi et al., 2000; Wallis et al., 2001; Bunge et al., 2003). It has been proposed that this abstract representation of task rule within the PFC biases processing throughout the rest of the brain by selectively enhancing activity of brain areas that encode the task-relevant information (Miller and Cohen, 2001). This is supported by neuroimaging studies in humans demonstrating rule-dependent interaction between PFC and posterior sensorimotor regions responsible for task execution (e.g., Stroop, 1935; Sakai and Passingham, 2003; Egner and Hirsch, 2005; Sakai and Passingham, 2006; Chiu et al., 2011; Miller et al., 2011; Nelissen et al., 2013; Waskom et al., 2014), and transcranial magnetic stimulation studies in humans showing disruption of PFC causally modulates the neural activity in posterior sensory cortex (Higo et al., 2011; Zanto et al., 2011; Lee and D'Esposito, 2012).

This mechanism in which feedback from the PFC exerts influence over posterior regions to bias competition in favor of task-relevant sensory and motor representations is well established (for reviews, see Miller, 2000; Ridderinkhof et

al., 2004). It is not clear, however, whether the same mechanism can be applied to situations in which the competition is among abstract representations of task rules. In such a case, both the source of the bias signal and the target of that signal could be within PFC. When multiple task rules are simultaneously activated, analogous to when multiple sensory stimulus or motor response representations are activated, how is this competition resolved? It is an important issue because the mechanism responsible for resolving conflicts between representations of non-sensory information might be different from those resolving conflicts between sensory representations of stimuli (for a review, see Kastner and Ungerleider, 2000) or between potential actions (for a review, see Cisek and Kalaska, 2010).

In the current study, we used functional magnetic resonance imaging (fMRI) to investigate the mechanism by which we can select relevant over irrelevant task rules. If the mechanism were similar to that which is thought to govern selection of sensory and motor representations (Desimone, 1998; Miller and Cohen, 2001), then we would expect to find two specific results. First, conflict between abstract rules would be expected to result in behavioral impairment and be accompanied by increased activity in a cognitive control network that helps to overcome the behavioral impairment. Second, conflict among abstract representations would be expected to be resolved by feedback from the prefrontal regions representing the currently relevant rule to the non-sensory and non-motor brain areas processing the abstract information needed

to perform the task according to that rule, enhancing relevant information, and perhaps secondarily inhibiting irrelevant information.

Participants were extensively trained so that strong associations were formed between different cue dimensions and one of two abstract task rules. Conflict was manipulated by having different cue dimensions (color and shape) associated either with the same task rule (congruent) or different ones (incongruent). Participants switched between two tasks according to the rule given by the currently relevant cue dimension, which was instructed at the beginning of each block and alternated across blocks. Phonological and semantic tasks were used, as they were previously shown to preferentially activate distinct brain areas (Sakai and Passingham, 2006; Lau and Passingham, 2007), allowing us to measure the degree of conflict between relevant and irrelevant rules, and the effect of top-down modulation that resolves this conflict. By using these abstract rules combined with trial-unique words to which the rules were applied, participants could not learn a specific stimulus-response association, but rather needed to resolve the conflict at a more abstract level of representation.

2.2. Materials and Methods

Participants. Sixteen (12 females, 4 males) right-handed, healthy young adults between 18 and 35 (mean age 20 ± 2.5 years) participated the study. All participants were native English speakers with normal or corrected-to-normal vision, no history of head injury, substance abuse, neurological or psychiatric

disorders, and were not taking any medications at the time of the study. The protocol was approved by the Institutional Review Boards of the Johns Hopkins University and the Johns Hopkins Medical Institutions. All participants provided written informed consent.

Experimental procedure. Participants were asked to make either a phonological or a semantic judgment for a visually presented word, as quickly as possible, while maintaining accuracy. We chose these semantic and phonological tasks because previous studies have shown that they preferentially activate distinctive regions within the frontal cortex (McDermott et al., 2003; Sakai and Passingham, 2006). This enabled us to use the blood oxygenation level dependent (BOLD) activity in these task-selective areas as a proxy for measuring the degree to which the relevant versus the irrelevant rule representations were activated by the task cues. The phonological rule required the participants to indicate, by pressing one of two buttons, whether the presented word contained two syllables or not. The semantic rule required the participants to indicate whether the meaning of the word referred to a concrete object or not. Left/Right button response mappings were counterbalanced across participants. To equate difficulty between the two task rules, the word stimuli were selected using criteria similar to that of Sakai and Passingham (2006). All the word stimuli were nouns with written frequency over 15, taken from the Medical Research Council Psycholinguistic Database (http://websites.psychology.uwa.edu.au/school/MRCDatabase/uwa_mrc.htm). Half of the words had two syllables and the other half had one or three syllables;

half had abstract meaning with a concreteness rating below 300 and the other half had concrete meaning with a concreteness rating above 500, according to the database. Different word stimuli were used in the pre-task training, scanning session, and localizer scans. Furthermore, the word stimuli in the scanning session (320 words) and localizer scans (144 words) appeared only once without repetition. This approach ensured that participants could not learn a specific stimulus-response association, but rather had to maintain the relevant rule at a more abstract level.

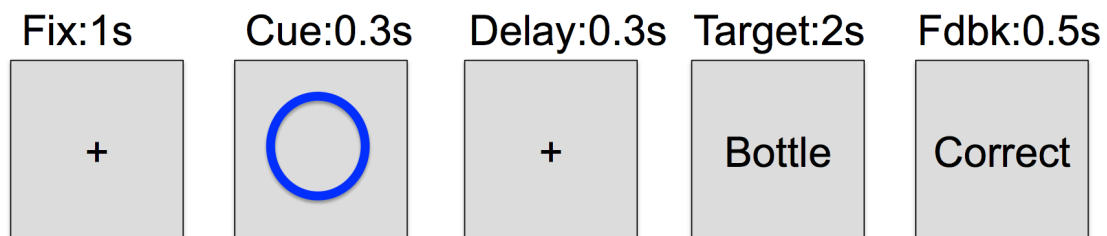
Training sessions. An example trial is illustrated in Figure 2.1. The applicable rule to apply was indicated by a task cue presented at the beginning of each trial. Importantly, participants trained on the two dimensions of the task cue (color and shape) on a computer prior to the scanning session. There were two separate training sessions, one for each cue dimension. In the color training session, participants responded according to the color dimension of the cue (e.g., green indicates the semantic task and blue indicates the phonological task), and in the shape training session, participants responded according to the shape dimension of the cue (e.g., circle indicates the semantic task and triangle indicates the phonological task). The task cue meaning and the rule assignment for both training sessions, as well as the order of the training sessions were counterbalanced across participants. Task instruction and a brief practice consisting of 24 trials were given at the beginning of each training session to make sure the participants understood the stimuli and procedures. Participants were instructed to respond according to the relevant cue dimension (i.e., either

shape or color), which remained constant over the entire course of the training sessions. To ensure both feature dimensions of the cue were strongly associated with their corresponding tasks, participants performed 320 trials over the course of 30 minutes on each dimension (an hour in total for both the color and shape training sessions) in a quiet laboratory room. A self-paced break was provided after every 64 trials. For each trial, the sequence began with a 300-ms task cue indicating the upcoming task, followed by a 300 ms delay. A target word then appeared and remained on screen until a response was made or the 2000 ms time limit was reached. After each response, feedback was presented for 300 ms to indicate whether the response was “Correct”, “Incorrect” or “Too slow”. The next trial began after a fixed interval of 3000 ms.

Functional magnetic resonance imaging (fMRI) session. After the training sessions, participants performed a brief practice of 64 trials outside of the scanner approximately 20 minutes before the scan began. Inside the scanner, participants performed 5 runs of 64 trials of the same semantic and phonological judgments. For each run, both in the practice and during scanning, trials were blocked into four “Color Blocks” (color was the relevant dimension), which alternated with four “Shape Blocks” (shape was the relevant dimension). Blocks were separated by a 11s rest period during which a fixation cross was presented. A 2-second instruction screen was presented at the beginning of each block (“Attend Color” or “Attend Shape”) to inform the participants of the relevant cue dimension for that block. After the instruction screen, eight trials were presented using the identical trial sequence as previously described for the training phase,

with the exception that the target word remained on the screen for the entire 2000 ms. Participants were told to focus on that cue dimension until the next instruction screen was presented. There were equal numbers of trials for the eight experimental conditions based on the relevant cue dimensions (color or shape), congruency of the cue (congruent or incongruent) and tasks (phonological or semantic), and the conditions were fully-crossed with left versus right response buttons, number of switch versus repeat trials, and whether the correct response for the target word for one task was the same or different as the correct response for that word according to the other task. The participants held one response button box in each hand, which sent the responses to a Cedrus RB-610 Response Box (Cedrus, San Pedro, CA) via fiber optic cables. Reaction time was measured from the onset of the target word until a response was made.

(A)



(B)

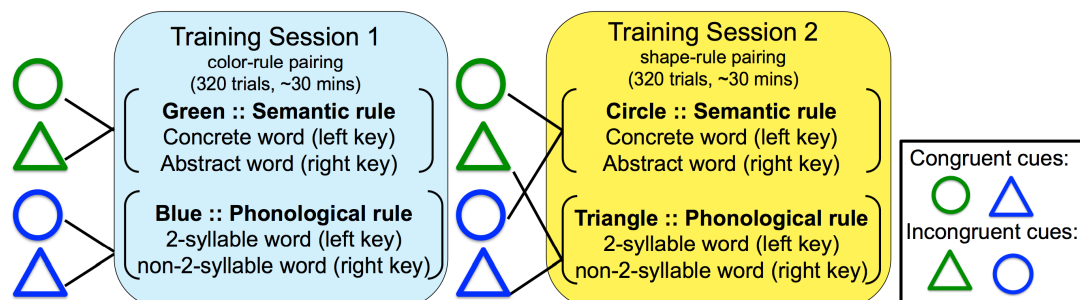


Figure 2.1. Example of trial events progression (A) and schematic drawing of task cues and their associated task rules (B). Each task cue had two dimensions: color and shape. For a given cue, each dimension could either be associated with the same task rule (congruent cues) or with different task rules (incongruent cues). During the training phase, the participants only needed to respond according to one of the two cue dimensions for the entire training session (320 trials), and then to repeat the same procedure based on the other cue dimension (320 trials). During the scanning session, the relevant cue dimension was instructed at the beginning of each block (“Attend Color” or “Attend Shape”). The relevant dimension remained constant within a block (8 trials per block), but alternated across blocks.

Functional localizer. The scanning session ended with functional localizer runs to independently identify brain regions preferentially activated during the use of phonological and semantic rules for every participant. During the localizer runs, participants performed phonological and semantic tasks in alternating blocks. Each localizer task sequence began with the presentation of a 2000ms instruction screen (“Syllable”, “Concrete”) indicating the upcoming task, which was followed by a 1000 ms preparation period and then by six trials of the corresponding task. Verbal instruction cues (“Syllable” for phonological task and “Concrete” for semantic task), rather than the colored shape cues, were used to avoid cue congruency effects. Within each block, word stimuli were presented for 1700 ms with a 300-ms inter-trial interval. Participants were instructed to

respond while the word stimulus was on the screen. A brief 1000-ms feedback indicating the overall performance for that block was given at the end of each block. Participants completed two runs of localizer task, each lasting 4.9 minutes. Each run consisted of 12 blocks (6 blocks of the semantic task alternated with 6 blocks of the phonological task), interleaved with 8 s of rest when participants passively viewed a fixation cross.

fMRI data acquisition and pre-processing. fMRI scanning was conducted at the F. M. Kirby Research Center for Functional Brain Imaging in Kennedy Krieger Institute (Baltimore, MD) on a 3.0T Philips Intera scanner equipped with 32-channel SENSE head coil. High-resolution T1-weighted anatomical images were collected using a MP-RAGE sequence (150 axial slices, TR = 7.9 ms, TE = 3.7 ms, flip angle = 8°, matrix = 212 x 172, voxel size of 1 x 1 x 1 mm). Whole brain T2*-weighted functional images were collected in an ascending sequential fashion, using an echo-planar imaging sequence (35 axial slices, TR = 2000 ms, TE = 3.7 ms, flip angle = 70°, in-plane resolution of 2.5 mm in 80 x 80 matrix, slice thickness = 2.5 mm, with a 0.5mm gap).

All preprocessing and statistical analyses were done using SPM8 (Wellcome Trust Centre for Neuroimaging). The first 6 volumes of each run were discarded to allow for scanner equilibration. The remaining functional image volumes were corrected for differences in slice acquisition timing using *sinc* interpolation, realigned to the first image volume to correct for head motion. The anatomical image was first co-registered to the mean of the motion-corrected functional images, and then it was segmented and spatially normalized to the

tissue probability maps included in the SPM8 toolbox using both linear and non-linear transformations. The normalization parameters (i.e. deformation field) derived from the anatomical image were then applied to all the functional images. In this step, the functional images were re-sampled to the same dimension (1.5 mm cubic voxels) as the anatomical images. Finally, the functional images were smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian kernel. Temporal autocorrelation was corrected using a first-order autoregressive model, and low-frequency drifts were removed using a high pass filter with a cutoff of 256 seconds (a cutoff of 100 seconds was used for functional localizer runs).

Behavioral analyses. Paired *t*-tests were used to compare reaction time (RT) and accuracy for trials associated with incongruent cues to those for trials associated with congruent cues. Additional *t*-tests were conducted to determine whether the behavioral congruency effect (RT difference between incongruent cues and congruent cues) changed as a function of task switching (switch versus repeat), block type (attend color versus attend shape), or tasks (phonological versus semantic task). All RT analyses were limited to the correct trials. The statistical threshold was set at $p < 0.0167$ (alpha = 0.05, two-tailed, Bonferroni corrected for multiple comparisons) for all behavioral analyses.

Voxelwise general linear model (GLM). Task-dependent changes in BOLD signal were modeled using separate regressors representing each possible combination of the block type (color, shape), cue congruency (congruent, incongruent) and task rule (phonological, semantic). Each regressor was time-locked to the onset of the task cue. In addition, error trials, the two

instruction screens informing the upcoming relevant cue dimension, and six head-motion parameters were included in the model as regressors-of-no-interest. All regressors, except those for the head-motion, were modeled by stick functions and convolved with SPM's canonical hemodynamic response function. The GLM model was estimated for each participant separately using SPM's first-level, fixed-effect, analysis. The primary contrast of interest was created for each participant to identify voxels exhibiting greater BOLD responses on all incongruent cue trials compared with congruent cue trials. All contrasts created at the subject-level were entered into a group-level random-effect analysis using a one-sample *t*-test against a contrast value of zero at each voxel. The statistical maps were thresholded using a voxel-level threshold of $p < 0.005$, corrected for multiple comparisons at a cluster-level of $p < 0.05$ (family-wise error correction). The cluster-extent threshold was calculated based on Gaussian random field method implemented in SPM8 (Friston et al., 1994).

Region of interest analysis. Functional regions of interest (ROIs) were chosen to test for interactions between PFC and task-selective areas. Because there was a high degree of variation across participants, the task-selective ROIs were identified in each participant using an independent functional localizer task. For the functional localizer, the statistical analysis was performed on the smoothed and normalized data. Two regressors of interest indicating the type of task for that block (semantic task, phonological task) as well as six head-motion parameters as regressors-of-no-interest were included in a GLM. The blocks were modeled as epochs spanning across the entire duration of the 16-second

block, which was then convolved with SPM's canonical hemodynamic response function. The GLM model was estimated for each participant separately using SPM's first-level fixed-effect analysis. Contrasts of interest were (1) phonological task > semantic task, and (2) semantic task > phonological task.

Additionally, the localization focused on the left premotor gyrus (PM) along the border of the inferior frontal gyrus (BA6/44) and the anterior portion of the left ventrolateral prefrontal cortex (aVLPFC) in BA47, because these areas have previously shown to be preferentially activated by the use of phonological rules versus semantic rules, respectively (Sakai and Passingham, 2006). To ensure each participant's task-selective ROIs were within these pre-specified areas (left PM and left aVLPFC), we used the group-level results to constrain the selection of subject-specific voxels. For the phonology-sensitive area, we selected voxels that (1) exceeded a threshold of $p < 0.05$ (uncorrected) in the phonological task greater than semantic task contrast in that participant, and (2) was within the left PM binary mask generated from the group-level random-effect analysis ($p < 0.05$, FWE-corrected) for the same contrast. Similarly, for the semantic-sensitive area, we selected voxels that (1) exceeded a threshold of $p < 0.05$ (uncorrected) in the semantic task greater than the phonological task contrast in the individual participant, and (2) was within the left aVLPFC binary mask generated from the group-level random-effects analysis ($p < 0.05$, FWE-corrected) for the same contrast. The peaks for PM (-50, -8, 44) and aVLPFC (-46, 28, -10) in our group analysis are consistent with what others have previously reported for these tasks (McDermott et al., 2003; Sakai and Passingham, 2006).

For each subject-specific ROI identified using the localizer scans, we extracted the beta values separately for each of the eight conditions from the first-level GLM of the main task. Since there were no significant differences in behavior or fMRI activation for color versus shape blocks, and our primary interest was the congruency effect on task-selective areas, we pooled the beta values across block types, resulting in 4 beta values per participant for each condition (phonological task/incongruent cue; phonological task/congruent cue; semantic task/incongruent cue; semantic task/congruent cue). Beta values for these four conditions were averaged across voxels within each ROI using MarsBaR toolbox (Brett, 2002).

One main hypothesis to be tested in the current study was whether the type of interactions that occur between the PFC and sensory or motor regions during selection also occur within the PFC itself, by biasing neural processing towards the prefrontal neurons coding abstract information needed for the relevant task rule over the irrelevant one. Previous research in visual attention has shown the selection can be achieved in sensory and motor regions by enhancing relevant information, suppressing irrelevant information, or a combination of both (Cohen et al., 1990). To delineate the precise mechanisms by which the PFC resolves conflicts among abstract task rules, we first identified the prefrontal region that showed significant activation using the incongruent > congruent contrast in the group-level analysis. This contrast identified a single cluster in the right inferior frontal gyrus (rIFG). Next, we calculated for each participant the extent to which activity in the task-relevant area was increased

during incongruent relative to the congruent trials (“enhancement index”), as well as the degree to which activity in the task-irrelevant area was decreased during the incongruent relative to the congruent trials (“suppression index”) using beta values. For each index, a larger score indicates the greater enhancement or suppression in the task-relevant or task-irrelevant areas, respectively. We then tested for a correlation between these indices and the activity changes in rIFG (incongruent – congruent) across participants, separately for each task condition. The hypothesis to be tested was whether greater activity in the rIFG during incongruent trials would be associated with greater enhancement of relevant abstract information, suppression of irrelevant abstract information, or both.

In addition to rIFG, previous studies have suggested that parietal cortex is part of the cognitive control network and its activity increases concurrently with PFC when participants actively maintain a relevant task rule in working memory (Brass and von Cramon, 2002; Bunge et al., 2003) and when participants switch rules from one task to another (Sohn et al., 2000; Braver et al., 2003; Yeung et al., 2006). Thus, we also identified a region in the right inferior parietal lobule (rIPL) using the incongruent > congruent contrast and performed the same across-participant correlation analysis within that region.

Multi-voxel Pattern Analysis (MVPA). The across-participant correlation analyses tested whether rIFG provides a top-down signal that helps to resolve conflict between abstract representations of task rules, by modulating activities in areas that process the abstract task information (semantic vs. phonological

information). To further investigate the representational content of this top-down signal from rIFG, we used MVPA to test whether the pattern of activity within rIFG contains rule information, context information, or both. This analysis was also performed in rIPL for comparison.

MVPA was performed using a linear support vector machine (LinearCSVMC) from LIBSVM library (Chang CC, 2011) implemented within the PyMVPA software package (Hanke et al., 2009). The preprocessing procedure included slice-timing and head movement correction. The resulting functional images were then smoothed with a 4 mm FWHM kernel. To reduce the problem related to BOLD signals overlapping across temporally adjacent events, a univariate GLM analysis was conducted to derive condition-specific beta estimates for each block. For each participant, beta values pertaining to either the semantic task or the phonological task were estimated in each of the 40 blocks, yielding two beta maps for each block. Trials were modeled as events time-locked to the onset of the cue using a stick function, which was then convolved with a canonical HRF. A constant of one for each of the 40 blocks was included in the model to remove the mean signal within each block. Error trials were excluded from analyses. In a separate GLM, a similar procedure was used to estimate beta values related to the color and shape contexts. Context here was functionally defined as the relevant cue dimension participants were cued to attend to within each block. Each of the eight trials within a block contributed to the estimation of beta value for that context, yielding one beta map for each block. Overall, these GLM analyses yielded 40 beta maps for each task

condition (phonological, semantic), and 20 beta maps for each context condition (color, shape).

Classifications of task rules and contexts were performed separately within the rIFG and rIPL clusters derived from the incongruent > congruent contrast. Each ROI was transformed back to the participant's native space by applying the inverse of the normalization parameters. This allowed us to conduct pattern classifications without re-sampling the individual beta maps to standard space. For each participant, the pattern of beta values within each ROI was extracted from each of the relevant beta maps. A leave-one-run-out procedure was used for cross-validation. A classifier was trained using the beta maps from four of the five runs and then tested using the beta maps from the held-out run. Five iterations were performed so that each run was tested once. The mean classification accuracy for each individual was determined by averaging the results across five iterations. To assess whether the classification performance was significantly different from chance (50%) at the group level, we first performed the permutation testing for each individual. This was done by randomly shuffling the target feature labels in the training sets (test set was not included) 5000 times to simulate the null distribution for a single participant. From the single-subject null distribution, we then randomly selected one classification accuracy from each participant, averaged these across the participants, and repeated this step 5000 times to build the group-level null distribution. The group-level significance was determined by comparing the

correct-label accuracy to the permuted-label accuracies at the level of $p < 0.05$ (two-tailed).

2.3. Results

Behavioral results

Overall, participants were significantly slower in the incongruent trials (Mean = 1145 ms, SD = 27 ms) relative to the congruent (Mean = 1108 ms, SD = 26 ms) trials ($t(15) = 3.341$, $p = 0.004$). Error rate was also significantly larger in the incongruent (Mean = 0.073, SD = 0.01) than the congruent (Mean = 0.053, SD = 0.008) trials ($t(15) = 2.991$, $p = 0.009$), indicating the congruency effect on RTs was not a result of speed-accuracy trade-offs. In addition, the observed congruency effect was not significantly different between phonological and semantic tasks ($t(15) = 0.948$, $p = 0.358$), between “Attend Color” and “Attend Shape” blocks ($t(15) = 0.052$, $p = 0.959$), between switch trials versus repeat trials ($t(15) = 0.183$, $p = 0.858$), or between congruent versus incongruent response trials based on the target word ($t(15) = 1.931$, $p = 0.073$). These behavioral results indicate that the congruency experimental manipulation resulted in rule conflict as intended, with no interaction from other potential factors such as relevant cue feature or the particular primary task to be performed.

Voxelwise GLM results

To identify the cognitive control networks involved in the resolution of conflicting abstract task representations, we performed a whole brain univariate analysis contrasting the incongruent trials to the congruent trials. Complementary to the behavioral congruency effects, a number of regions demonstrated greater activation in the incongruent condition compared to the congruent condition, including rIFG, right insula, rIPL, right putamen, right postcentral gyrus, right precuneus, and midbrain (Figure 2.2). The opposite contrast (congruent > incongruent) did not yield any significant activation differences. Of particular note, the rIFG cluster located in the ventrolateral prefrontal cortex (MNI coordinates of peak: 48, 28, 15; BA 45/46) has been previously implicated in tasks that require inhibition of irrelevant task sets or overriding a pre-potent response (Aron et al., 2003; Aron et al., 2004).

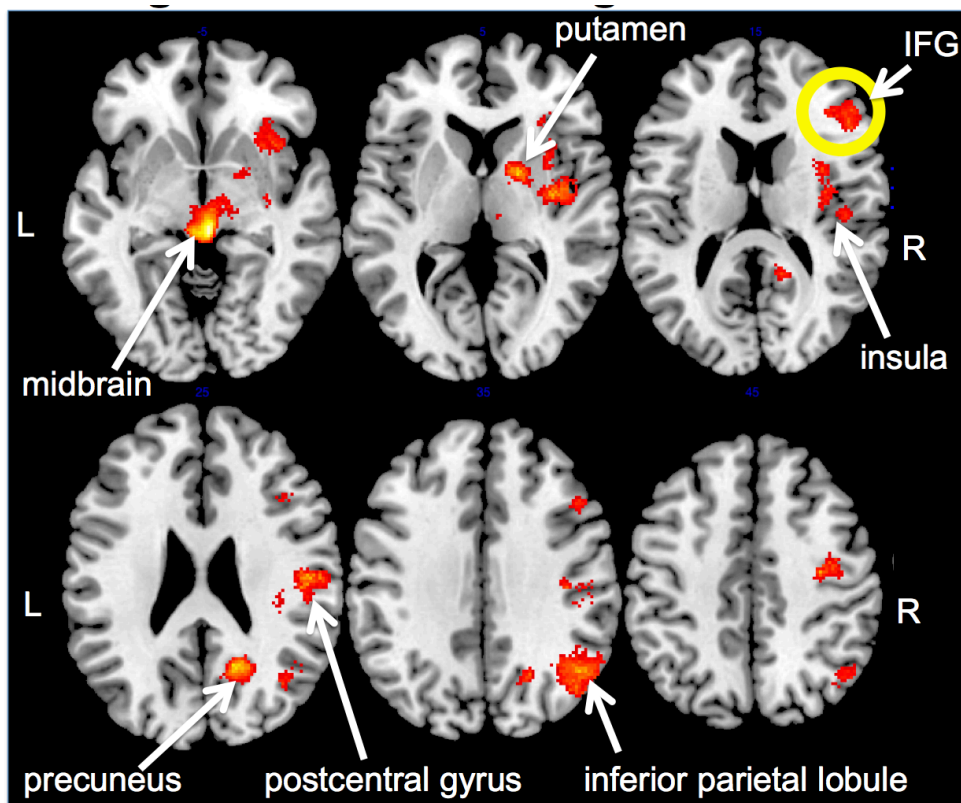


Figure 2.2. Regions showing greater activation in the incongruent condition compared to the congruent condition.

Congruency effects on task-selective areas

We first examined the congruency effect in areas preferentially active for the phonological or the semantic task using ROIs independently identified during the separate functional localizer scans. Since we only analyzed correct trials where the conflict between task rules should have been mostly resolved by the time a motor response was made, we might have expected to see a strong activation in task-relevant areas (i.e. left PM for the phonological task and left aVLPFC for the semantic task), and minimal activation in task-irrelevant areas (i.e. left PM for the semantic task and left aVLPFC for the phonological task) equally for both incongruent and congruent conditions. Alternatively, if the competition had not been completely resolved, then we would expect to see more activation in the task-irrelevant area and less activation in the task-relevant area during incongruent trials than during congruent trials.

To test these predictions, the beta values for these two ROIs were extracted and plotted as a function of relevant tasks and cue congruency (Figure 2.3). Two repeated-measures ANOVAs were conducted to test for an interaction between cue congruency (congruent, incongruent) and task (semantic, phonological) separately for each ROI. As expected because these ROIs were functionally defined using the localizer scans, activity in the left PM ROI was greater in the phonological task condition than the semantic task condition (F

(1,15) = 8.429, $p = 0.011$), whereas the opposite pattern was observed in the left aVLPFC ROI ($F(1,15) = 21.963$, $p < 0.001$). There was no significant interaction between congruency and task in either ROI (left PM, $F(1,15) = 0.231$, $p = 0.638$; left aVLPFC, $F(1,15) = 0.406$, $p = 0.142$). The absence of an interaction effect is consistent with the hypothesis that the conflict between task rules was at least partially resolved shortly after the cue presentation.

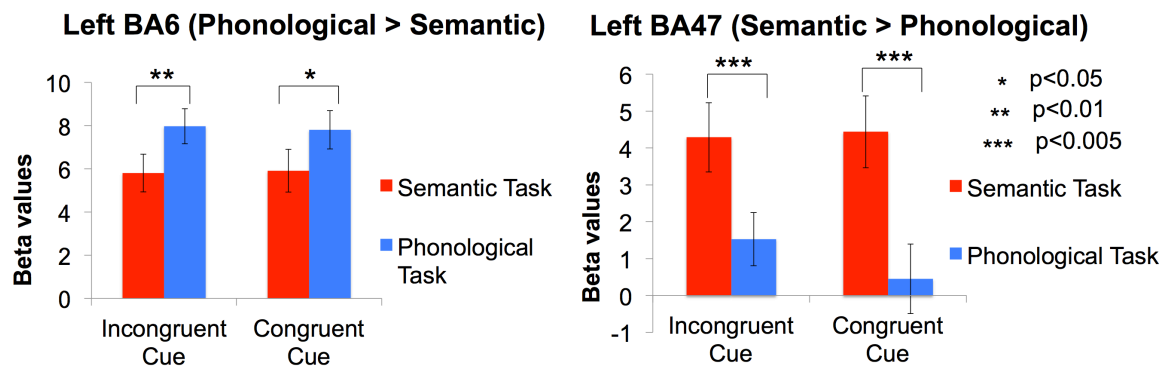


Figure 2.3. During correct trials, the congruency of the cue did not appear to change the amount of activation in either the relevant or irrelevant task areas (both interaction results show $p > 0.05$), indicating the competition was at least partially resolved.

Across participants correlation between rIFG and task-selective areas

Although there was no interaction between congruency and the amount of activation in task-relevant and irrelevant areas in the group-level ROI analyses, the possibility remained that the degree to which the conflict between task rules was resolved on incongruent trials could have been different across participants,

and that this could be related to the degree to which an individual activated the rIFG. Indeed, this is what we found using an across-participant correlation analysis. As shown in Figure 2.4, the degree to which rIFG activation was increased during the incongruent trials relative to the congruent trials predicted the size of the enhancement effects in the task-relevant areas for the phonological task (left PM, $r = 0.79$, $p < 0.001$) and for the semantic task (left aVLPFC, $r = 0.546$, $p = 0.029$), but not the size of the suppression effects in the task-irrelevant areas for either the phonological task (left aVLPFC, $r = -0.333$, $p = 0.208$) or the semantic task (left PM, $r = -0.399$, $p = 0.126$). The same correlation analysis was also performed in rIPL. The size of the increase in rIPL during incongruent compared to congruent trials did not predict the size of the enhancement in the task-relevant areas for the phonological task (left PM, $r = 0.237$, $p = 0.376$) or for the semantic task (left aVLPFC, $r = 0.426$, $p = 0.1$), nor did it predict the size of the suppression in the task-irrelevant areas for the phonological task (left aVLPFC, $r = -0.401$, $p = 0.124$) or for the semantic task (left PM, $r = 0.022$, $p = 0.936$). These results provide support for the theory that regions within PFC can be both the source of biasing signals and the target of those signals. Furthermore, the data indicates that this resolution of conflict among abstract task rules is accomplished by the enhancement of activity in brain areas representing relevant abstract information, rather than by the suppression of activity in areas representing irrelevant abstract information.

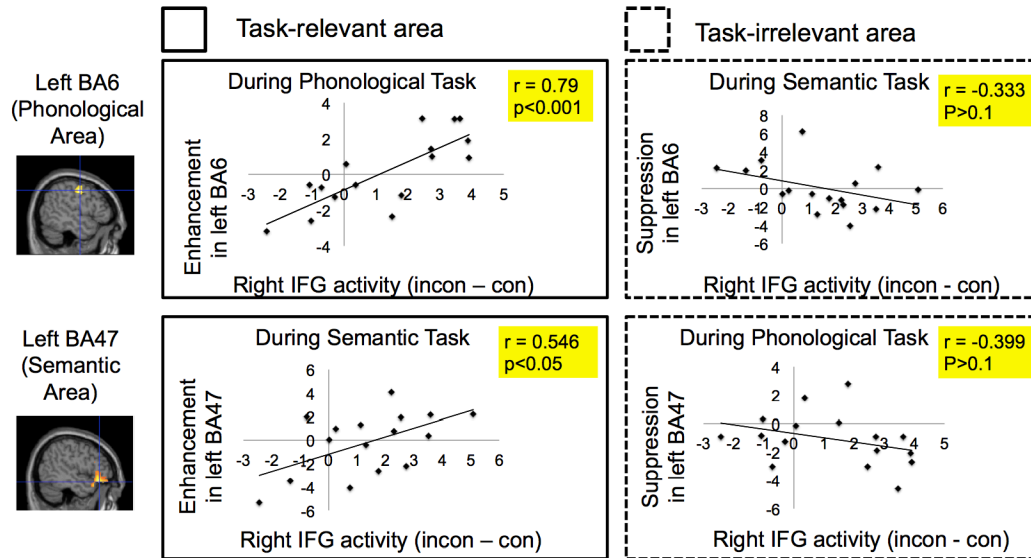


Figure 2.4. Top two graphs show data from the left BA6 region that was preferentially activated for the phonological task. The bottom two graphs show data from the left BA47 region that was preferentially activated for the semantic task. Graphs on the left show individual differences in the degree of activation enhancement in the task relevant area (BA6 for the phonological task and BA47 for the semantic task) as a function of that participant's activation difference in the rIFG for incongruent versus congruent trials. Graphs on the right show individual differences in the degree of activation suppression in the task-irrelevant area, again as a function of the incongruent versus congruent activation of the IFG. Enhancement is defined as the difference in betas for the incongruent trials minus the congruent trials, and suppression is defined as the difference in betas for the congruent trials minus the incongruent trials.

MVPA Results

MVPA analysis was performed to investigate the nature of the neural population code in rIFG that enables it to act as a bias signal. The results were in line with the hypothesis that patterns of activity in rIFG contain both the relevant rule information (mean classification accuracy for semantic versus phonological trials = 57.06%, $p < 0.001$) and contextual information (mean classification accuracy for color versus shape blocks = 54.22%, $p = 0.019$). For comparison, we also conducted another MVPA using patterns of activity from rIPL. The pattern of activity in rIPL yielded a significant classification result for the rule information (mean classification accuracy = 55.23%, $p < 0.001$), but not for the contextual information (mean classification = 52.27%, $p = 0.123$). To summarize, our results indicate that both rIPL and rIFG contain information about the current task rule, but only rIFG activation also contains information about the context and only the rIFG activation is correlated with the degree to which the task-relevant information is enhanced.

2.4. Discussion

We used functional neuroimaging techniques to examine the mechanism responsible for resolving conflict between abstract representations pertaining to task rules: selecting the relevant abstract task rule over the irrelevant one. In previous studies, the mechanism by which conflict between task sets was resolved was indirectly tested by measuring activity in task-relevant and task-irrelevant brain regions during task switching (Yeung et al., 2006) and during conflict adaptation (Egner and Hirsch, 2005). However, one unexplored avenue

in previous work was that the conflict in the tasks used in those studies could have occurred at multiple levels of processing, ranging from stimulus representations, response representations, to rule representations. Thus, an important feature of the current study is that the rule conflict was manipulated independently of the sensory features of the task cues or any motor planning responses triggered by the targets, enabling us to manipulate the degree of conflict at the task-rule level. In the current study different features of the task cues were associated with either the same (congruent cues) or different task rules (incongruent cues). Both congruent and incongruent cue stimuli had both color and shape feature dimensions. The context instruction at the beginning of the block unambiguously indicated which feature dimension was relevant. The conflict arose on incongruent trials only because of the learned association between the irrelevant cue dimension and the irrelevant abstract task rule, not because of conflict at the sensory level itself. Furthermore, we used a unique target word for each trial to prevent learning of an association between the target word and a specific response. Thus, conflict at the response level was also minimized.

Behaviorally, we found task performance was slower and less accurate in the incongruent condition relative to the congruent condition, suggesting that additional control processes were required following incongruent cues. These behavioral results provide strong evidence that our congruency manipulation was successful. Using functional neuroimaging, we also demonstrated that the behavioral congruency effect was accompanied by greater BOLD activity in a

network of regions commonly associated with cognitive control and conflict resolution, including lateral prefrontal cortex, parietal cortex, insula, and subcortical areas.

The primary goal of the current study was to test whether the mechanisms involved in resolving conflict among abstract representations within the PFC were similar to those involved in resolving conflict among as they do with sensory and motor representations. It is widely believed that the PFC serves as a source of top-down control over other brain areas to bias processing towards goal-relevant sensory and motor information (Miller and Cohen, 2001). Thus, we predicted that conflict between abstract representations of task rules would be resolved by prefrontal feedback to the brain areas processing the goal-relevant, abstract information. A previous study showed that when participants were subliminally primed to perform a different task than the one that was explicitly instructed, activity decreased in the brain area selective for the instructed (relevant) task and activity increased in the brain area selective for the primed (irrelevant) task (Lau and Passingham, 2007). The changes of activity during incongruent trials relative to congruent trials, in both that study and the current study, can be thought of as an index of the degree to which the participants engaged in the irrelevant task. In Lau and Passingham's (2007) study, the magnitude of irrelevant task activation was only apparent when the conflicting task cue was low visibility and participants were thus unaware of the conflict. In the current study, using highly visible task cues, we found the congruency of the task cues did not appear to change the overall strength of activation in either the task-relevant or task-

irrelevant area, when activation differences were assessed in the group analysis, consistent with the previous result. However, when assessing individual differences in the responses during incongruent and congruent trials, a different interpretation emerged. The interesting question here was whether the difference in activity between the incongruent and congruent conditions for the task-relevant and task-irrelevant areas changes as a function of the degree to which different participants recruited PFC during incongruent trials. We tested this hypothesis by looking for correlations between the activation changes in task-selective areas and activation changes in (1) the rIFG, a functionally defined cognitive control locus within the ventrolateral PFC, and (2) in the rIPL, another functionally defined cognitive control region that is frequently concurrently activated with PFC during performance of cognitive control tasks (Bunge et al., 2003; Crone et al., 2006; Yeung et al., 2006), and has been implicated in providing top-down modulation when the task requires spatial attention to particular location (Kastner et al., 1999; Corbetta et al., 2000).

Specifically, we found that, across participants, the degree to which the rIFG increased during the incongruent condition relative to the congruent condition predicted the magnitude of the enhancement effect in the task-relevant area but not the suppression effect in the task-irrelevant area. This correlation between the rIFG and task-relevant area activations was significant regardless of which of the two task rules was currently relevant. On the other hand, we did not find a significant correlation between rIPL activation and task-selective areas for either task. These observed relationships provide important insights about how

conflict between abstract rule representations is resolved and how it may be similar to or different from conflict resolution mechanisms in sensory and motor cortices. Classic models of “biased competition” for selective attention include both enhancement of relevant information and mutually inhibitory interactions that result in a winner-take-all outcome. While the original models were developed primarily based on single cell electrophysiological data, fMRI studies have also found evidence for suppression of irrelevant sensory information by selective attention within visual areas (Kastner et al., 1998). For the abstract representations within PFC in the current study, such suppression, if it exists, appears much smaller than the enhancement of relevant information. It is important to note, however, that the suppressive interaction among multiple visual stimuli is a result of direct lateral inhibitory connections within a single functional area. Suppression of activity related to irrelevant visual stimuli occurs when those stimuli are within the receptive fields of the same neurons. The neural activity patterns related to the different types of abstract representations in the current study (i.e. left PM and left aVLPFC) reside in separate brain areas that likely do not share strong inhibitory connections with each other. Thus, the enhancement of neural activity in one area would not necessarily be expected to result in inhibition of the other. Overall, our data are in agreement with previous selective attention studies that showed competing sensory stimuli were resolved through enhancement of task-relevant target information, including selective attention between spatial locations (Heinze et al., 1994; Luck et al., 1997), stimulus features (Corbetta et al., 1991; Chawla et al., 1999) and objects

(O'Craven et al., 1999; Serences et al., 2004). These previous studies demonstrated resolution of sensory-based stimulus conflict through neural enhancement of brain areas coding the relevant sensory information. The current study extends these findings by showing that feedback from specific prefrontal regions coding the currently relevant task rule enhances the relevant information needed to perform that task, even when that relevant information is neither sensory nor motor and is represented by neural populations that are also within the prefrontal cortex. Furthermore, the lack of a significant correlation for rIPL also suggests that rIFG may be the primary loci of cognitive control that provides top-down modulation when it comes to resolution of conflict among abstract representations. The rIPL may provide feedback more specifically for the control of sensory representations.

To better understand the nature of the bias signal from rIFG, we conducted MVPA to investigate the representational content within this area. One possibility was that rIFG could have represented information about the currently relevant rule, which then would drive increases of activity in brain areas that code the abstract information pertaining to that relevant rule. Alternatively, rIFG could have represented the currently relevant contextual information (i.e., color or shape block). This contextual information, combined with particular cue-stimulus input, could have, in turn, driven changes of activity in brain areas representing the abstract information pertaining to the rule. Other alternatives were that rIFG could have represented both rule and contextual information, or neither. Successful MVPA classification indicates that the patterns of activity

within this region spatially encode information about the representational content of interest. Our results indicate that rIFG represents both contextual and rule information. In contrast, the rIPL appears to represent rule information, but not context. The MVPA results are consistent with previous studies that showed IPL was involved in retrieving and maintaining rule information in working memory (Bunge et al., 2003; Crone et al., 2006). In relation to the across-participant correlation result, however, it appears that rIPL is not the source of the top-down signal that biases competition of abstract representations towards the relevant one. The results indicate that rIFG biases selection of the appropriate abstract task representations according to both the cue and the current, more temporally extended context. In contrast, the currently relevant rule representations, or perhaps the bound sensory features of both color and shape that were presented to instruct the relevant rule for the current trial, may be represented in the rIPL, but it does not appear to play a direct causal role in the selection of the relevant over the irrelevant abstract information.

In conclusion, we have shown that when there is conflict between abstract rules, rIFG mediates that conflict by enhancing activity in brain areas representing relevant information, rather than by suppressing activity in brain areas representing irrelevant information. The rIFG has previously been implicated in multiple types of cognitive control processes, including motor inhibition (Aron et al., 2004) and reflexive attentional reorienting (Corbetta et al., 2008). Previous research has also suggested that different subregions of rIFG could have different roles in cognitive control (for review see Waskom et al.,

2014). The current study suggests a general mechanism by which this region might exert these multiple types of control, namely by integrating recent (cue) and more temporally distant (context) information in order to represent information needed to selectively enhance other relevant information in the presence of conflicting irrelevant information, regardless of whether that information is sensory, motor, or abstract.

3. Chapter 3: Separate Cognitive Control Resources Recruited for Resolving Switching- vs. Congruence-induced Rule Conflicts

3.1. Introduction

To achieve behavioral goals, cognitive control permits flexible use of limited cognitive resources by configuring information processing according to the currently relevant task rule. This control is particularly important when the task rules are frequently shifting or when resolution of conflicting task rules is required. One central question regarding cognitive control is how the brain determines that cognitive control is needed and then brings those resources to bear in order to resolve the conflict. The conflict-monitoring account proposes that the demand of cognitive control may be evaluated by a conflict-monitoring unit (the anterior cingulate cortex), which detects any type of conflict in information processing and then relays the conflict signal to a strategic control unit (the dorsolateral prefrontal cortex), which then resolves conflict by enhancing the task-relevant information (Botvinick et al., 2001). By this account, the conflict-monitoring unit is sensitive to the general level of conflict, regardless the way in which conflicts might be generated. Recently, such a “domain-general” conflict-control account has been called into question. Several studies have combined different types of conflict, such as stimulus-based Stroop conflict and response-based Simon conflict, to assess whether control processes triggered by one type of conflict facilitated the resolution of another (Egner et al., 2007). It was shown that the conflict-driven control mechanisms recruited by one type of conflict does not affect the resolution of another. Moreover, the stimulus-based

Stroop conflict modulated the activity in parietal cortex and the response-based Simon conflict modulated the activity in premotor area. Such a pattern of results support a conflict-specific cognitive control account in which separate control resources are recruited to resolve each type of conflict independently. If conflict among sensory representations and motor representations are resolved via their own cognitive control resources, then this evokes the question whether different sources of conflict regarding abstract representations of non-sensory rule information might be resolved in a similar conflict-specific manner.

The mechanism of cognitive control for resolving conflict associated with task rules has been extensively studied using cued task-switching paradigms (e.g., Logan and Zbrodoff, 1979; Sohn et al., 2000; Crone et al., 2006; Yeung et al., 2006) or congruence paradigms that utilize bivalent stimuli, i.e., stimuli with features associated with two different tasks (e.g., Duncan-Johnson and Kopell, 1981; Botvinick et al., 2001; Bunge et al., 2002; Brass and von Cramon, 2004; Kunde and Wühr, 2006; Kim et al., 2013). The former paradigm requires the participant to frequently switch between two or more task rules based on the instruction given by a task cue (e.g. perform either parity or magnitude judgments on digits based on the cue presented) while the latter requires the participants to remember the current context to select between two possible tasks evoked by the two dimensions of the bivalent stimulus (e.g. in Stroop task, the color evokes color naming task and the word evokes word reading task, and the relevant task is dependent on the current context). Thus, in both cases, there is a conflict between a relevant and an irrelevant task rule, and participants are required to

select the relevant rule to meet the current behavioral goal. However, the source of conflict originates differently. In the task-switching paradigm, the conflict arises from the residual activity related to a previously performed task rule (Allport et al., 1994; Yeung et al., 2006) and the control process related to setting up for the new task and disengaging from the previous task (Rogers R.D., 1995; Monsell, 2003). In a congruence paradigm, however, the conflict arises when different dimensions of the stimulus are simultaneously mapped onto conflicting rule representations (Kornblum et al., 1990; Kornblum and Lee, 1995). Hence, an unanswered question is whether different sources of conflict involved in task rules are associated with dissociable, conflict-specific cognitive control mechanisms or whether a single, domain-general cognitive control mechanism is responsible for resolving all types of task conflict. According to the conflict-specific account, each source of task conflict would be resolved via its own dedicated cognitive control mechanism, each of which operates independently from the other. In contrast, according to a domain-general account, a single cognitive control mechanism would work flexibly to resolve all sources of task conflict.

In the current study, we wanted to examine the generality of cognitive control mechanisms for resolving different sources of task conflict, namely the switching-induced and the congruency-induced task conflicts. Task conflict is defined as competition between rules that differ in their cognitive operations, which occur regardless of the overlap among sensory stimuli and among responses.

To identify and directly compare the cognitive control processes for resolving switching-induced versus congruence-induced task-rule conflicts, we deployed two strategies. First, we used the same data as was collected for the results reported in Chapter 2, for which the task involved conflict between task rules that was manipulated independently of the sensory features of the task cues or any motor planning response triggered by the targets. This was done through training participants to associate different dimensions (color and shape) of the cue with either the same rule (congruent cues) or different ones (incongruent cues), combined with the use of trial-unique words to which the rules were applied. This allowed us to examine the cognitive control mechanisms for as-pure-as-possible task rule representations, which had not been possible in previous studies (Bunge et al., 2003; Yeung et al., 2006). Second, specific to the goal of examining the specificity of conflict resolution control mechanism, we independently manipulated task switching (switch/repeat) and cue congruency (incongruent/congruent) using a factorial design within a single experimental protocol. This allowed us to directly assess differential neural activation involved in resolving switching-induced versus congruency-induced conflict.

3.1.1. Materials and Methods

The same data set as Chapter 2 was used for this investigation; therefore all task, stimulus and participant information is identical. It is repeated here for the reader's ease of reference.

Participants. Sixteen (12 females, 4 males) right-handed, healthy young adults between 18 and 35 years of age (mean 20 ± 2.5) participated the study. All participants were native English speakers with normal or corrected-to-normal vision, no history of head injury, substance abuse, neurological or psychiatric disorders, and were not taking any medications at the time of the study. The protocol was approved by the Institutional Review Boards of the Johns Hopkins University and the Johns Hopkins Medical Institutions. All participants provided written informed consent.

Experimental Procedure. Participants were asked to make either a phonological or a semantic judgment for a visually presented word, as quickly as possible, while maintaining accuracy. The phonological rule required the participants to indicate, by pressing one of two buttons, whether the presented word contained two syllables or not. The semantic rule required the participants to indicate whether the meaning of the word referred to a concrete object or not. Left/Right button response mappings were counterbalanced across subjects. To equate difficulty between the two task rules, the word stimuli were selected using criteria similar to that of Sakai and Passingham (2006). All the word stimuli were nouns with written frequency over 15, taken from the Medical Research Council Psycholinguistic Database (http://websites.psychology.uwa.edu.au/school/MRCDatabase/uwa_mrc.htm). Half of the words had two syllables and the other half had one or three syllables; half had abstract meaning with a concreteness rating below 300 and the other half had concrete meaning with a concreteness rating above 500, according to

the database. Different word stimuli were used in the pre-task training and scanning session, and none of the word stimuli was repeated during the scanning session.

Training sessions. The purpose of the training sessions was to experimentally manipulate the conflict level associated with the task cue. An example trial is illustrated in Figure 3.1. The applicable rule to apply was indicated by a task cue presented at the beginning of each trial. Importantly, participants trained on the two dimensions of the task cue (color and shape) on a computer prior to the scanning session. There were two separate training sessions, one for each cue dimension. In the color training session, participants responded according to the color dimension of the cue (e.g., green indicates the semantic task and blue indicates the phonological task), and in the shape training session, participants responded according to the shape dimension of the cue (e.g., circle indicates the semantic task and triangle indicates the phonological task). The task cue meaning and the rule assignment for both training sessions, as well as the order of the training sessions were counterbalanced across participants. Task instruction and a brief practice consisting of 24 trials were given at the beginning of each training session to make sure the participants understood the stimuli and procedures. Participants were instructed to respond according to the relevant cue dimension (i.e., either shape or color), which remained constant over the entire course of the training sessions. To ensure both feature dimensions of the cue were strongly associated with their corresponding tasks, participants performed 320 trials over the course of 30

minutes on each dimension (an hour in total for both the color and shape training sessions) in a quiet laboratory room. A self-paced break was provided after every 64 trials. For each trial, the sequence began with a 300-ms cue indicating the upcoming task, followed by a 300 ms delay. A target word then appeared and remained on screen until a response was made or the 2000 ms time limit was reached. After each response, feedback was presented for 300 ms to indicate whether the response was “Correct”, “Incorrect” or “Too slow”. The next trial began after a fixed interval of 3000 ms.

Functional magnetic resonance imaging (fMRI) session. After the training sessions, participants performed a brief practice of 64 trials outside of the scanner approximately 20 minutes before the scan began. Inside the scanner, participants performed 5 runs of 64 trials each of the same semantic and phonological tasks. For each run, both in the practice and during scanning, trials were blocked into four “Color Blocks” (color was the relevant dimension), which alternated with four “Shape Blocks” (shape was the relevant dimension). Blocks were separated by a 11s rest period during which a fixation cross was presented. A 2-second instruction screen was presented at the beginning of each block (“Attend Color” or “Attend Shape”) to inform the participants of the relevant cue dimension for that block. After the instruction screen, eight trials were presented using the identical trial sequence as previously described for the training phase, with the exception that the target word remained on the screen for the entire 2000 ms. Participants were told to focus on that cue dimension (color or shape) until the next instruction screen was presented. There were equal numbers of

trials for the four experimental conditions based on the congruency of the cue (congruent or incongruent) and task switching (switch or repeat), and the conditions were fully-crossed with number of phonological task versus semantic tasks and left versus right response buttons. Switch and repeat trials were defined within the context of a color or shape block. The first trial of every block was eliminated from the analysis, because the switching or repeating of the color/shape context for those initial trials would have added noise to the analysis. The participants held one response button box in each hand, which sent the responses to a Cedrus RB-610 Response Box (Cedrus, San Pedro, CA) via fiber optic cables. Reaction time (RT) was measured from the onset of the target word until a response was made.

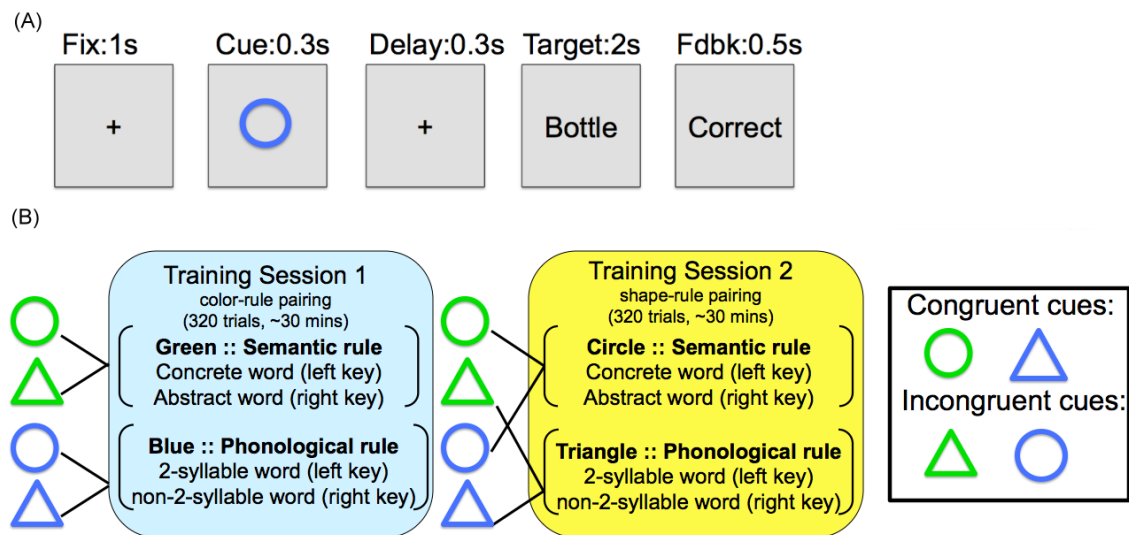


Figure 3.1. (A) Example of trial events progression, and (B) schematic drawing of task cues and their associated task rules. Each task cue had two dimensions: color and shape. For a given cue, each dimension could either be associated

with the same task rule (congruent cues) or with different task rules (incongruent cues). During the training phase, the participants only needed to respond according to one of the two cue dimensions for the entire training session (320 trials), and then to repeat the same procedure based on the other cue dimension (320 trials). During the scanning session, the relevant cue dimension was instructed at the beginning of each block (“Attend Color” or “Attend Shape”). The relevant dimension remained constant within a block (8 trials per block), but alternated across blocks.

fMRI data acquisition and pre-processing. fMRI scanning was conducted at the F. M. Kirby Research Center for Functional Brain Imaging in the Kennedy Krieger Institute (Baltimore, MD) on a 3.0T Philips Intera scanner equipped with 32-channel SENSE head coil. High-resolution T1-weighted anatomical images were collected using a MP-RAGE sequence (150 axial slices, TR = 7.9 ms, TE = 3.7 ms, flip angle = 8°, matrix = 212 x 172, voxel size of 1 x 1 x 1 mm). Whole brain T2*-weighted functional images were collected in an ascending sequential fashion, using an echo-planar imaging sequence (35 axial slices, TR = 2000 ms, TE = 3.7 ms, flip angle = 70°, in-plane resolution of 2.5 mm in 80 x 80 matrix, slice thickness = 2.5 mm, with a 0.5mm gap).

All preprocessing and statistical analyses were done using SPM8 (Wellcome Trust Centre for Neuroimaging). The first 6 volumes of each run were discarded to allow for scanner equilibration. The remaining functional image volumes were corrected for differences in slice acquisition timing using *sinc* interpolation, realigned to the first image volume to correct for head motion. The

anatomical image was first co-registered to the mean of the motion-corrected functional images, and then it was segmented and spatially normalized to the tissue probability maps included in the SPM8 toolbox using both linear and non-linear transformations. The normalization parameters (i.e. deformation field) derived from the anatomical image were then applied to all the functional images. In this step, the functional images were re-sampled to the same dimension (1.5 mm cubic voxels) as the anatomical images. Finally, the functional images were smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian kernel. Temporal autocorrelation was corrected using a first-order autoregressive model, and low-frequency drifts were removed using a high pass filter with a cutoff of 256 seconds.

Behavioral analyses. A 2x2 ANOVA with “cue congruency” (congruent/incongruent) and “task switch” (switch/repeat) as within-subject factors was performed on both the RT and accuracy data. Because the first trial of each color or shape block cannot be categorized as either a switch or a repeat trial, we excluded these trials as well as error trials from all behavioral analyses. The statistical threshold was set at $p < 0.05$ (two-tailed).

To investigate whether individuals who are better at switching between rules also are better at resolving incongruence of the cue, an across-participant correlation analysis was performed between the switch cost (switch trial RT – repeat trial RT) and the incongruency cost (incongruent trial RT – congruence trial RT) for the 16 participants.

Voxelwise General Linear Model (GLM). Task-dependent changes in BOLD signal were modeled using separate regressors for each of the four conditions (incongruent_switch, incongruent_repeat, congruent_switch, congruent_repeat). In addition, the first trial on every block, error trials, the two instruction screens informing the upcoming relevant cue dimension, and six head-motion parameters were included in the model as regressors-of-no-interest. All regressors, except those for the head-motion, were modeled by stick functions and convolved with SPM's canonical hemodynamic response function. The general linear model was estimated for each participant separately using first-level (fixed-effect) analysis. For each participant, contrasts were created for each of the four experimental conditions using a one-sample t test against a contrast value of zero (i.e. the experimental conditions versus implicit baseline (fixation)). The four first-level individual contrasts were then included in the corresponding cells in the second-level (random-effect) factorial design. A 2 x 2 full factorial design was used with "cue congruency" and "task switch" as two within-subject factors. Statistical t -test maps were constructed for all switch trials compared with repeat trials, and for all incongruent trials compared with congruent trials, and interaction of the two factors. The statistical maps were thresholded using a voxel-level threshold of $p < 0.005$, corrected for multiple comparisons at a cluster-level of $p < 0.05$ (family-wise error correction). The cluster-extent threshold was calculated based on Gaussian random field method implemented in SPM8 (Friston et al., 1994).

Conjunction analysis. To examine whether the neural circuit involved in the main effect of switching and the neural circuit involved in the main effect of cue congruency overlap with each other (i.e. whether there are common brain regions are involved for both effects), we further performed a conjunction analysis (Nichols et al., 2005) using SPM “conjunction null” option. By performing a statistical test on the intersection of two thresholded statistical maps, a conjunction analysis reveals whether there is brain region commonly activated across tasks. Both contrasts (Switch > Repeat, Incongruent > Congruent) were thresholded at $p < 0.071$ for the conjunction analysis, which renders an overall threshold at $0.071 \times 0.071 = 0.005$.

Furthermore, we performed two additional conjunction analyses to investigate possible overlap in activations between the interaction effect and the main effect of incongruence cues ($\text{incongruent_switch} > \text{congruent_switch}$) > ($\text{congruent_rep} > \text{incongruent_rep}$) \cap ($\text{incongruent} > \text{congruent}$), and between the interaction effect and the main effect of task switching ($\text{incongruent_switch} > \text{congruent_switch}$) > ($\text{congruent_rep} > \text{incongruent_rep}$) \cap ($\text{switch} > \text{repeat}$).

Region of interest analyses. To further characterize the activation profile in the clusters identified by the interaction contrast from the GLM analysis, region-of-interest (ROI) analyses were performed. Parameter estimates were extracted from each ROI and averaged across the area using Marsbar (Brett et al., 2002). Planned paired *t*-tests on simple main effects were performed with an alpha of 0.05.

3.1.2. Results

Behavioral results

For the RT data, 2-way ANOVA revealed a significant main effect of cue congruency on RT ($F(1,15) = 9.77$; $p = 0.006$): participants were slower on incongruent trials compared to congruent trials (1140 vs. 1108 ms), and a main effect of task switch ($F(1,15) = 27.117$; $p < 0.001$): participants were slower on switch trials compared to repeat trials (1159 vs. 1089 ms). However, there was no significant interaction ($F(1,15) = 0.009$; $p = 0.924$) between cue congruency and task switch (Figure 3.2). No significant correlation was found between switch cost and incongruence cost ($r = -0.03$, $p = 0.902$) across participants.

For the accuracy data, there was a main effect of cue congruency ($F(1,15) = 9.654$; $p = 0.006$): participants were less accurate on incongruent trials than on congruent trials (92.67% vs. 94.7%), but accuracy did not differ significantly ($F(1,15) = 1.354$, $p = 0.261$) between the switch and repeat trials (92.96% vs. 94.4%). The interaction was marginally significant ($F(1,15) = 3.883$, $p = 0.065$), showing that the cue congruency effect was slightly greater for switch trials than repeat trials. Accuracy and RT data were shown in Table 3.1 and Figure 3.2.

Table 3.1 Behavioral performance by trial type

	Trial Type			
	Con-Swt	Con-Rep	Incon-Swt	Incon-Rep
RT(sec)	1139(28)	1077(25)	1178(31)	1101(25)
Accuracy(%)	94.10(1.17)	94.92(0.85)	91.58(1.19)	94.19(1.12)

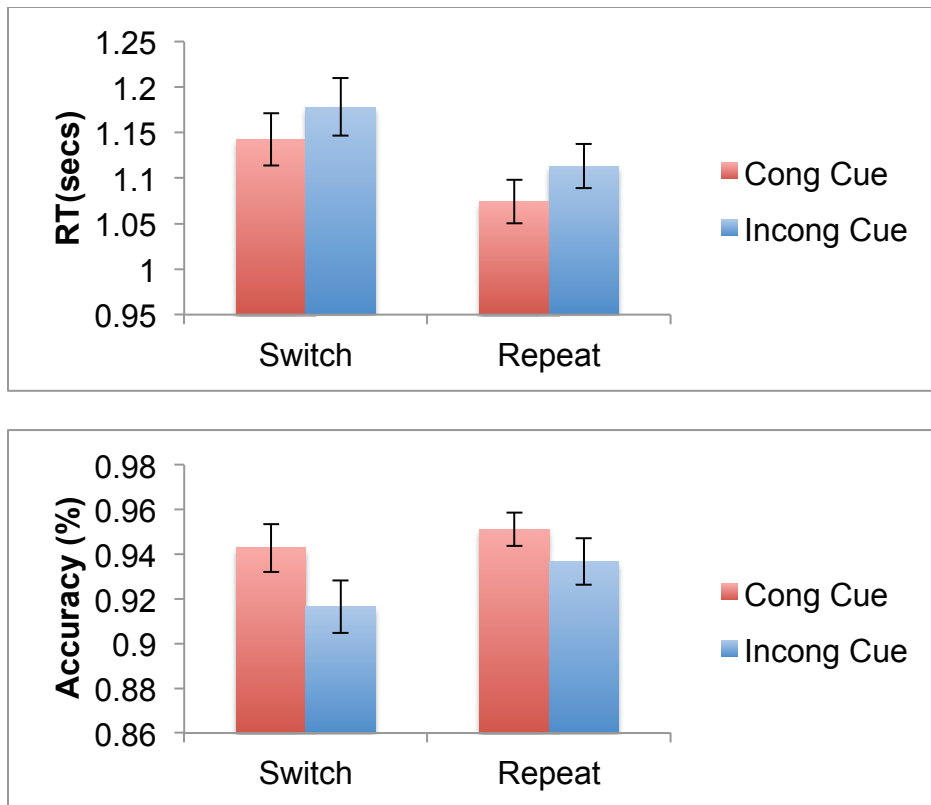


Figure 3.2. RTs and accuracy are plotted separately for congruent cue and incongruent cue trial, for both rule repetitions and rule switches. RTs are shown for correct responses only.

Neuroimaging results

Common and specific neural correlates underlying switching and congruency effects

We first identified brain areas associated with the main effect of switching between task rules. Figure 3.3 shows the results of Switch > Repeat contrast in blue color, which revealed a network of cognitive control regions that included left precentral gyrus, pre-supplementary motor area (pre-SMA)/SMA, and left inferior parietal lobule (IPL), left precuneus, and midbrain. No significant activation was

found in the reverse contrast. Next, we identified the brain areas associated with the main effect of cue congruency. The Incongruent > Congruent contrast (Figure 3.3, red color) revealed a network of regions that included anterior cingulate gyrus (ACC), right inferior frontal gyrus (IFG), right IPL, right insula, right precuneus, and midbrain. No significant activation was found in the reverse contrast.

A conjunction analysis was performed to identify whether there are common brain regions showing activation for both main effects of switching and cue congruency. The conjunction analysis between the “Incongruent > Congruent” AND “Switch > Repeat” contrasts revealed no significant activation overlap between these two contrasts, suggesting there was no common areas underlying these two main effects.

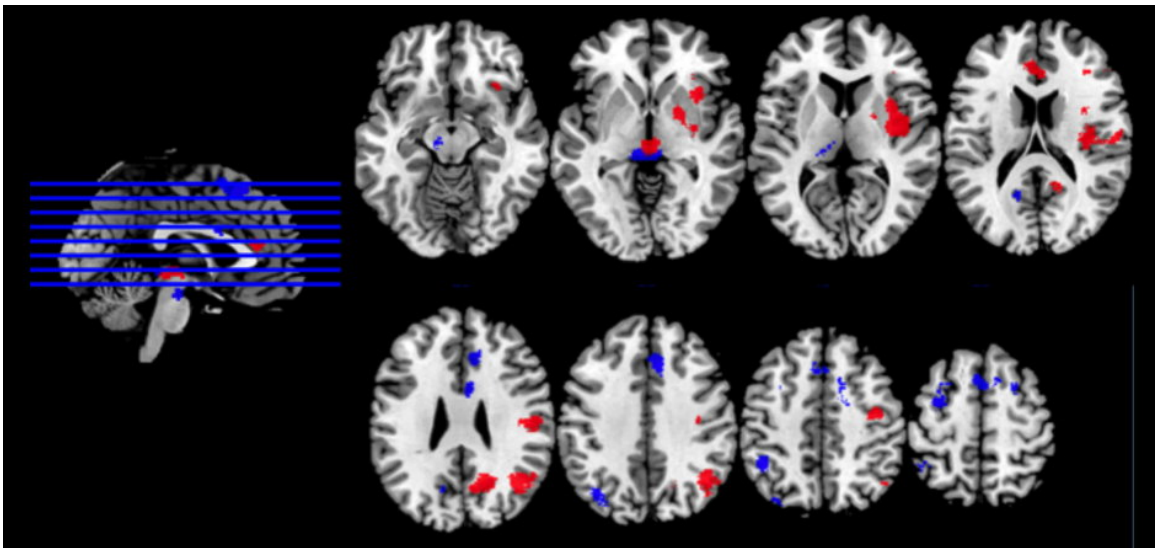


Figure 3.3. Areas active for resolving cue congruency (red) and for switching between task rules (blue).

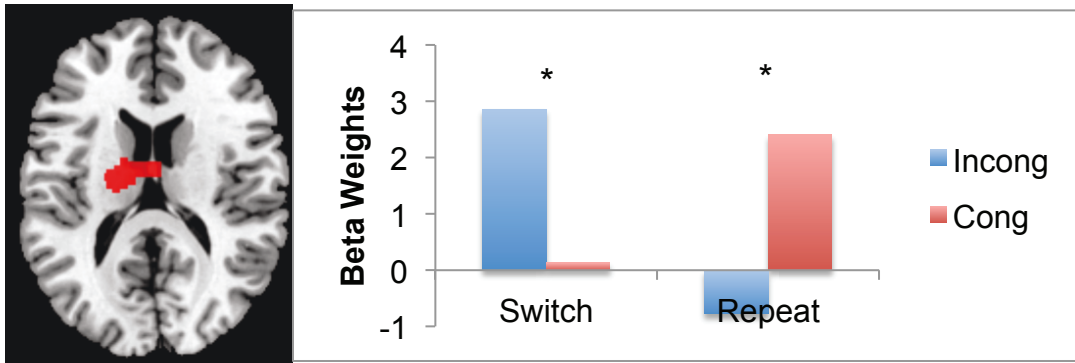
Neural interaction between switching and congruency.

The interaction contrast of between Switching (switch/repeat) and Congruency (congruent/incongruent) showed significant activation in left precentral gyrus (BA6, MNI: -32, -13, 66; $t(16) = 3.86$), the opercular part of left IFG (oper_IFG, MNI: -40, 14, 21; $t(16) = 3.64$), the orbital part of left IFG (BA47, MNI: -44, 21, -11; $t(16) = 3.93$), fusiform gyrus/Middle Occipital Gyrus (FG/MOG, MNI: 28, -82, -17, $t(16) = 3.56$), and thalamus (MNI: -2, -6, 16; $t(16) = 4.37$) (Figure 3.4). To understand what was driving these interactions, we then performed ROI analyses to examine the activation patterns within each cluster. These ROI analyses revealed that, for all ROIs, the increase in activity for incongruent over congruent trials was greater during switching (all p values < 0.05). In the thalamus, the congruency effect was actually reversed during repeat trials such that activity was significantly greater for congruent than incongruent conditions during repeat trials ($p = 0.009$). In the other ROIs, congruency effects were only marginally significant in the opercular IFG ($p = 0.059$), IFG/BA47 ($p = 0.059$), precentral gyrus ($p = 0.09$), and fusiform gyrus ($p = 0.062$). No significant activation was found in the reverse interaction contrast. Thus, these comparisons showed that all these areas were more active on incongruent trials compared to the congruent trials for the switch trials, but not for the repeat trials. The observed interaction was thus primarily attributable to a relative increase of activity on switch_incongruent trials compared to all other conditions.

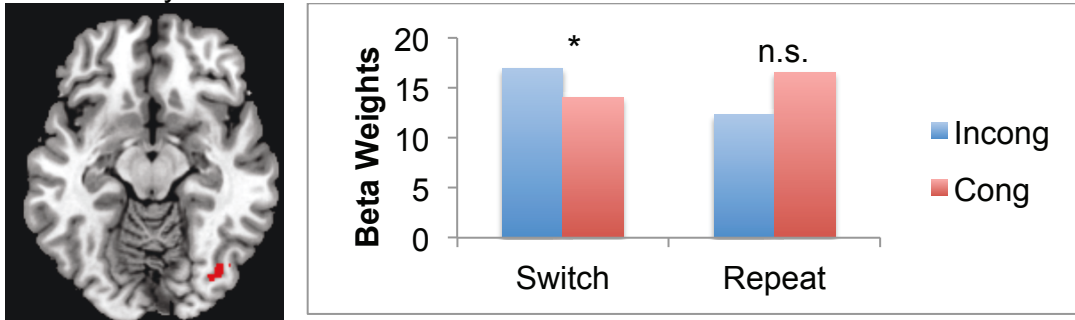
Finally, conjunction analyses were also performed to investigate possible overlaps in activations between interaction effects and each of the main effects (i.e. switch $>$ repeat, as well as incongruent $>$ congruent). The conjunction

analyses did not show any suprathreshold voxels, indicating that no area demonstrated both a main effect of either congruency or switching and an interaction between the two.

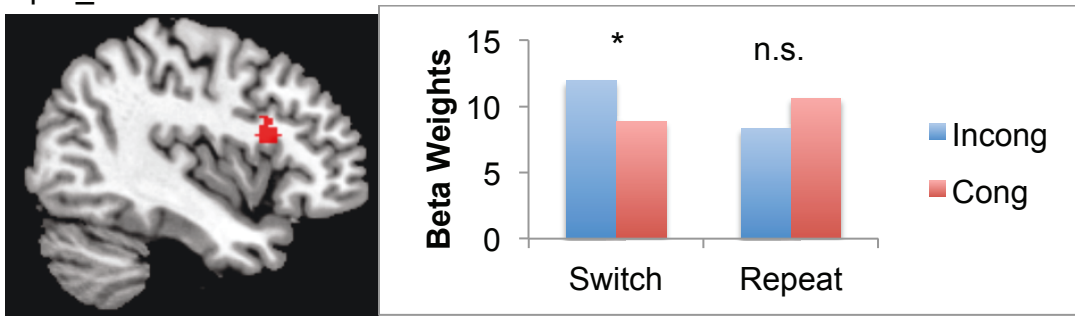
Thalamus



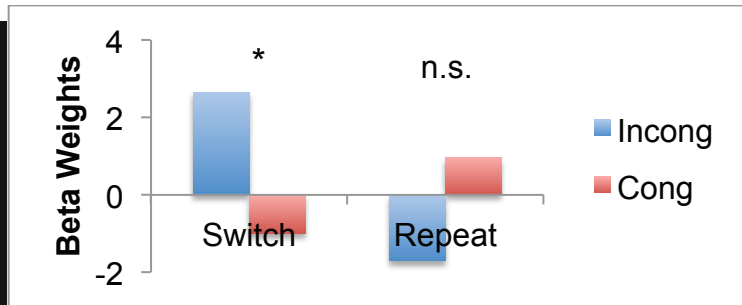
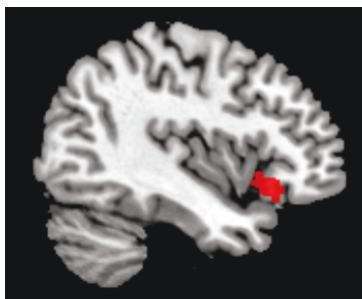
Fusiform Gyrus



Oper_IFG



IFG/BA47



Precentral Gyrus/BA6

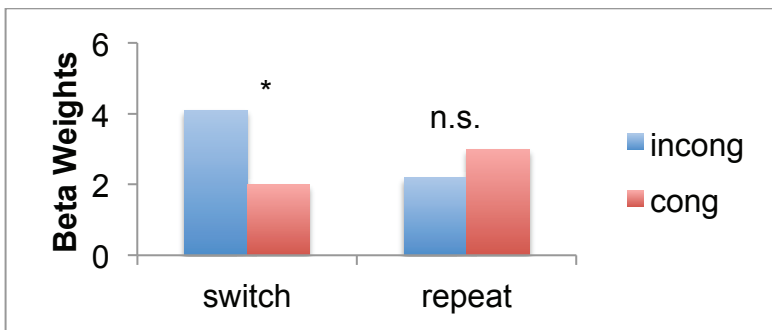
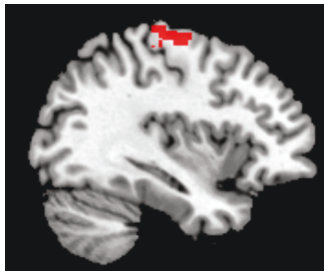


Figure 3.4. Neural interactions between task switching (switch/repeat) and cue congruency (incongruent/congruent). Left thalamus, left precentral gyrus, left orb_IFG, left oper_IFG, right fusiform gyrus were significantly activated by the interaction contrast “Switch (Incongruent > Congruent) > Repeat (Congruent > Incongruent). Beta weights in the four experimental conditions were extracted from the activated clusters and plotted. Abbreviation: IFG: inferior frontal gyrus; Oper_IFG: the opercular part of the inferior frontal gyrus.

3.2. Discussion

The cognitive control mechanism for conflict resolution regarding task rules has been commonly examined using either a task-switching paradigm or a congruence paradigm. In both paradigms, competition occurs between a

relevant and an irrelevant rule; however, the sources of the conflict are different.

In the present fMRI study, we show for the first time, by manipulating the levels of conflict for switching and congruency independently within a single paradigm, that these two sources of task conflict recruit different neural circuits for conflict resolution, implicating conflict-specific cognitive control mechanisms that work separately to resolve each task conflict types.

Regarding the behavioral data, we found a robust switch cost resulted from switching between two task rules across trials, this phenomenon is commonly reported in task-switching literature (for a review, see Monsell, 2003). In our experiment, the switch cost was 70 ms, and there was no significant difference of switch cost between the congruent and incongruent condition. The extra time needed for the switch trials is likely to reflect the time-consuming process of reconfiguring the brain system to engage the new task and/or disengage the old task (Rogers R.D., 1995) as well as the overcoming of “proactive” interference associated with the previously relevant but currently irrelevant task (Allport et al., 1994). Note that we recognize that the sources of switch costs has been hotly debated for decades (Monsell, 2003; Sakai, 2008), but we don’t make theoretical claims about what task-switching components contribute to the switch costs since they were not within the scope of this study.

In addition to the switch cost, a behavioral incongruence cost was also observed resulting from different rules being activated by the relevant dimension and the irrelevant dimension of the cue. The incongruence cost was measured 39 ms and there was no significant difference of incongruent cost for the switch

condition and the repeat condition. The manipulation of incongruent versus congruent cues at the task level by using trial unique target stimuli and no fixed stimulus-response mappings is a novel feature of our present study. By having participants associate different dimensions (color and shape) of the cue with either the same rule (congruent cues) or different ones (incongruent cues), combined with the use of trial-unique words to which the rules were applied, we ensure the conflict between task rules was manipulated independently of the sensory features of the task cues or any motor planning response triggered by the targets. As the currently appropriate context (color or shape) changes frequently across blocks, a momentary lapse of attention control can cause the involuntary processing of the task rule associated with the irrelevant cue dimension, which leads to conflict at a task-specific level and incongruence cost. Finally, we examined the interaction between these two sources of task-rule conflict. We found additive effects of switching-induced and incongruency-induced conflict, but not an interactive effect. Given that each conflict was manipulated independently in a factorial manner, the absence of interaction suggests a dissociation of the two sources of task conflict.

Once we established that the sources of the conflict are independent from each other behaviorally, we could then examine the neural data to answer the main question, concerning whether there are dissociable conflict-specific control mechanisms preferentially involved in resolving one source of task conflict over the other, or a single control mechanism flexibly involved in resolving different sources of task conflict. The fMRI results are in line with the conflict-specific

hypothesis: we found switching-induced and incongruency-induced conflict recruit distinct sets of brain regions. Specifically, the control-related brain regions sensitive to switching-induced conflict were primarily left-lateralized and included precentral gyrus, pre-SMA/SMA and IPL. On the other hand, the control-related brain regions sensitive to incongruency-induced conflict were primarily right-lateralized, and included ACC, IFG, IPL, and insula. Our conjunction analysis between the two main effect contrasts “Switch > Repeat” and “Incongruent > Congruent” showed that there is no anatomical overlap of activation specific to these two sources of conflict, which provides further support for the conflict-specific hypothesis.

Our finding that task switching activates a fronto-parietal network in the left hemisphere is consistent with previous studies (e.g. Badre and Wagner, 2006; Kim et al., 2011; Muhle-Karbe et al., 2014; Vallesi et al., 2015). In a recent study, Vallesi et al. (2015) demonstrated that the brain lateralization observed in task-switching is independent of the specific tasks to be performed (i.e., verbal or spatial). Interestingly, we also found cue incongruence activates a fronto-parietal network in the right hemisphere as well as ACC in the midline. According to the conflict-monitoring theory (Botvinick et al., 2001), the ACC detects the presence of conflict and sends signals to the dorsolateral prefrontal cortex (DLPFC), which in turn biases the system toward the task-relevant information. However, the right-lateralized front-parietal network involved in resolving task conflict induced by incongruent cues is an interesting finding. Previous studies have shown right IFG is directly involved in response inhibition (Aron et al., 2004, 2014). Similarly,

an Activation Likelihood Estimation meta-analysis of Go/No-go tasks also have reported a mainly right-lateralized network associated with response inhibition, including the IFG (BA44/45), IPL (BA40), and the superior medial frontal gyrus (BA6) (Buchsbaum et al., 2005). However, in our present study, we specifically eliminated conflict caused by learned stimulus-response associations by using different target words for every trial. In addition, the behavioral results also showed no effect of response congruency when we examined the RT associated with incongruent words (the correct response for the word is the same for either tasks) versus congruent words (the correct response for the word is different for either tasks) (the analysis was not shown in the current paper). Thus, the current study showed evidence that the right fronto-parietal network, particularly rIFG, may play a more general role of maintaining the context to bias selection of the relevant rule over the irrelevant ones, rather than response inhibition per se.

This lateralization that we observed in our study may reflect the sustained versus transient components of cognitive control processes needed for successfully resolving incongruency-induced and switching-induced conflict, respectively. Using a hybrid block and event-related paradigm, Braver et al. (2003) demonstrated that the sustained cognitive control component during task switching obtained from contrasting mixed-task blocks to single-task blocks primarily activates right-lateralized frontoparietal brain regions. In contrast, the trial-by-trial transient cognitive control component during task switching obtained from contrasting task-switch trials to task-repeat trials primarily activates left-lateralized frontoparietal brain regions. In relation to our study, to successfully

resolve the incongruency-induced conflict, participants were required to actively maintain the currently relevant context (color or shape) in working memory to bias selection of the relevant task rule. This is conceptually analogous to the sustained cognitive control process in which task contexts or multiple task sets are actively maintained in working memory. On the other hand, the switching-induced conflict is more likely to recruit a trial-by-trial transient control process that involves the internal reconfiguration of task set or updating the appropriate stimulus-response mappings. In this context, the distinct brain networks for resolving the switching-induced and incongruency-induced conflict that we found in our study may reflect two different modes of cognitive control – one requires sustained maintenance of context (color/shape) to select the appropriate rule for the current trial, and the other one requires flexible update of task rule representations.

In the whole-brain analysis, we obtained neural interaction effects between task switch and congruence in the precentral gyrus, IFG/BA47, the opercular section of IFG, and fusiform gyrus. Planned comparisons showed that these areas were more active on incongruent trials compared to the congruent trials for the switch trials, but not for the repeat trials. Therefore, the observed interaction was thus primarily attributable to a relative increase of activity on switch_incongruent trials compared to all other conditions. In addition, the conjunction analyses between the interaction effect and the two main effects showed no overlap of activations. Taken together, these patterns of results

suggest that these areas are only recruited when both switching and resolving incongruency of tasks are required.

In conclusion, by factorially combining task switching with cue congruency within a single design, our study revealed that there are distinct neural circuits involved in resolving conflict from switching between task rules and from choosing between conflicting task-rules according to context. These results support the “conflict-specific” hypothesis that different sources of task conflict recruit dissociable cognitive control networks. In addition, there were also areas that were preferentially engaged specifically when both types of conflict were present, but not when only one or the other was present, which lends support to the hypothesis that task-switching comprises neurally dissociable sub-processes.

4. Chapter 4: Modulation of Switch Cost and Incongruence Cost by Proportion Conflict Manipulation

4.1. Introduction

In the previous chapter, we have demonstrated that different types of task conflict, i.e. conflict induced by frequent switching between different task rules (switching-induced task conflict) and conflict induced by having stimulus features associated with two different task rules (incongruence-induced task conflict), recruit separate brain networks for conflict resolution. One remaining question is whether the recruitment of anatomically distinct brain networks indicates that different cognitive control mechanisms are involved for resolving switching-induced task conflict versus incongruence-induced task conflict. Previous literature on conflict resolution and cognitive control has described two forms of control, proactive and reactive control, that are separated in terms of their cognitive properties and brain activity (Braver et al., 2003; Braver et al., 2007). Proactive control is a sustained form of control that can be engaged when one anticipates occurrence of conflict, allowing rapid response by actively maintaining task-relevant information in working memory. Reactive control is a transient form of control that can be engaged when the occurrence of a conflict event is unpredictable and triggers the reactivation of required task-relevant information in a transient manner. Therefore, despite that both forms of control are adequate to correct task performance, there are some situations in which one mode of control is preferentially engaged. To answer the question whether different cognitive control mechanisms are involved in resolving switching- versus incongruence-induced conflict, we can modulate the task context to encourage the adoption of

proactive control for one conflict type, and test (1) whether such manipulation of cognitive control have equal effects on both conflict types and (2) whether control recruited by one type of conflict were to facilitate the resolution of the other conflict type.

Congruence cost and switch cost in task conflict

The complex and ever-changing environment we live in requires the human ability to select the appropriate behavioral option amidst other inappropriate competitors, as well as the ability to flexibly adapt our behavior to meet the new environmental demands. To achieve these, cognitive control configures information processing according to the currently relevant task rule that determines appropriate behavior. In the cognitive control literature, one common strategy used to study the mechanism of cognitive control is to measure task performance in incongruence tasks, where two different processing streams compete for behavior. For example, in a classical Stroop color naming task (Stroop, 1935; MacLeod, 1991), participants are required to name the color of the ink in which the words are printed. Reaction times (RTs) are reliably larger for trials in which the name of the printed word is incongruent with its color (e.g., the word RED printed in green) than it is not (e.g., the word RED printed in red). The difference of RT (incongruent – congruent) is often referred as the incongruence cost. While the incongruence cost found in the Stroop task is often thought to reflect response conflict due to the automaticity of reading (e.g. Duncan-Johnson and Kopell, 1981; Cohen et al., 1990; MacLeod, 1991), it has also been

suggested that task conflict partially contributes to the Stroop interference effects due to the fact that the word stimulus may, in itself, cue a reading task rather than the (required) color-naming task, regardless of the specific word (e.g. MacLeod and MacDonald, 2000; Brown and Besner, 2001; Goldfarb and Henik, 2007).

Another commonly used means to study cognitive control mechanisms, particularly in the context of task interference, is the task-switching paradigm (for a review, see Monsell, 2003). In this paradigm, participants are required to shift between two different tasks (either predictably or signaled by a cue). The RTs are reliably larger following a task switch (task A \rightarrow task B), compared with a task repeat (task A \rightarrow task A). The difference of RT between task-switch trials and task-repeat trials is referred as the switch cost, which provides a behavioral index of the control processes involved in reconfiguration of the brain state for the upcoming task as well as inhibition of the previous task set. The current study is aimed to understand whether there are different cognitive control mechanism for resolving task conflict in regards to the incongruence and task-switching costs.

According to the conflict monitoring theory (Botvinick et al., 2001), the adjustment of cognitive control is served by anterior cingulate cortex (ACC) which detects the presence of conflict within the system, and then relays the conflict signals to dorsolateral prefrontal cortex (DLPFC), which exerts top-down control by biasing information processing towards the task-relevant representations in other parts of the brain. Two well-known manipulations have been used as support for the conflict monitoring theory. The first, sequential conflict adaptation

effects are defined by a reduction in the interference effects on a current trial when preceded by an incongruent trial compared to when preceded by a congruent trial (Gratton et al., 1992). The second, proportion congruent effects are defined by a reduction in the interference effects in a block with a high proportion of incongruent trials, compared to a block with low proportion of incongruent trials (Logan and Zbrodoff, 1979). The same block-wise proportion manipulation can also be applied to task-switching paradigm by manipulating the frequencies of switch versus repeat trials. In general, smaller switching costs have previously been observed in blocks with high proportion of switch trials (75% switch and 25% repeat) compared to blocks with low proportion of switch trials (25% switch and 75% repeat) (e.g. Dreisbach et al., 2002; Dreisbach and Haider, 2006; Schneider and Logan, 2006).

Specificity of conflict control

One recurring issue with conflict control is the generality of the cognitive control across different conflict types. In the conflict-monitoring model, the conflict-control loop is considered to be “conflict-nonspecific”, such that the monitoring component is sensitive to the general level of conflict within the system, regardless of the conflict types. On the other hand, there have been studies arguing that conflict control can be conflict-specific. A number of studies have examined the specificity of cognitive control using proportion congruence and/or conflict adaptation effects in the context of combining interference tasks involving different conflict types (e.g. Kunde and Wühr, 2006; Egner, 2007;

Freitas et al., 2007; Verguts and Notebaert, 2009). For instance, Egner et al. (2007) combined two independent sources of conflict, stimulus-based conflict (Stroop) and response-based conflict (Simon), within a single experiment, and then assessed whether control processes triggered by one type of conflict transferred to the resolution of another. They found the control triggered by stimulus-based conflict on the previous trial resulted in resolution of stimulus-based conflict on the current trial, but did not result in resolution of conflict for the response-based conflict. Similarly, the control triggered by response-based conflict on the previous trial resulted in resolution of response-based conflict on the current trial, but did not result in resolution of conflict for the stimulus-based conflict. Their findings suggest that different types of conflict are probably mediated by independent conflict control loops that operate in parallel.

Another suggestion regarding the specificity of control is that the sequential conflict adaptation and proportion congruent effects could reflect different cognitive control mechanisms. For instance, Funes et al. (2010) combined a spatial Stroop task and a Simon task within a single paradigm. By comparing the two behavioral effects in their ability to reduce interference within the same conflict type versus across the other conflict type, they found proportion congruent effects generalized from one conflict type to another, whereas the sequential conflict adaptation effects seemed to be conflict specific. This dissociation was interpreted as evidence of different cognitive control mechanisms underlying the two effects. The authors further explained their results in the context of reactive and proactive control (Braver, 2012). On the

one hand, the proportion congruence effect may be related to sustained adjustment of cognitive control for a whole block rather than single trial. This modulation of cognitive control is most commonly attributed to the adoption of the so-called “proactive control” strategy (the sustained active maintenance of task-set information). Such proactive control is probably implemented after the participants have experienced the level of conflict on the first few trials in a block, which produces tonic changes to the neural pathways by enhancing the task-relevant representations. On the other hand, the sequential conflict adaptation effects operate on a trial-to-trial basis. Since the transient adjustment of control is implemented in a just-in-time manner following a high interference event, it likely reflects reactive control.

Task-switching cost and incongruence cost

While many studies investigate the specificity of cognitive control for conflict resulting from competing response (e.g. Simon effect), competing stimulus-response associations (e.g. the classical Stroop), and competing stimuli properties (e.g. Flaker), very little has known about conflict involves competing task rules. The present work fills this gap in the literature by focusing on two conflict types involves competition between task rules: task-rule incongruence and task-rule switching.

When using the aforementioned interference tasks to study cognitive control, one often encounters the issue that task conflict and response conflict are confounded to some degree. Therefore, we used a variant on the same task

paradigm that we developed for the studies reported in Chapters 2 and 3 that allows us to manipulate the level of conflict at the task level, independently from other sources of conflict, such as the sensory properties of the task cues (stimulus conflict) or motor responses triggered by the targets (stimulus-response conflict).

The current study

The main question addressed in the current study is whether the cognitive control system that resolves incongruence cost and the cognitive control system that resolves switching cost are merely anatomically separate, as previously shown in Chapter 3, or are they qualitatively distinct mechanisms. To test this, we modulated the task context to encourage the deployment of proactive control, so as to examine whether such manipulation affects costs associated with cue incongruence and task switching in a similar fashion or not. In addition, we tested whether proactive control triggers by manipulating the frequency of one conflict type has a domain general effect as suggested by conflict monitoring theory (Botvinick et al., 2001), or a conflict-specific effect.

To do this, first, we manipulated task congruence by introducing a training period in which participants were trained to associate different dimensions (color and shape) of the cue with either the same rule (congruent cues) or different ones (incongruent cues), combined with the use of trial-unique words to which the rules were applied. This allows us to examine the cognitive control mechanisms governing rule representations, independently of particular stimuli or

responses. Second, we independently manipulated task switching (switch/repeat) and cue congruency (incongruent/congruent) using a factorial design within a single experimental protocol. This allows us to determine whether these conflict types are independent from each other (i.e. non-interactive effects) such that resolution of one conflict type does not result in facilitation or impairment of conflict resolution of the other conflict type, or they are overlapping conflicts (i.e. interactive effect) such that resolution of one conflict type result in facilitation or impairment of conflict resolution of the other. Finally, cognitive control was modulated using a proportion manipulation to influence costs associated with cue incongruence and task switching. Switching-induced conflict and incongruence-induced conflict were manipulated separately such that when the ratios of task switches varied, the ratio of task-rule congruency was held constant and vice versa. This allows us to keep the general level of conflict constant across two conditions (i.e. switching-manipulated blocks and incongruence-manipulated blocks)

4.1.1. Method

Participants

Twenty-three (23) Johns Hopkins University undergraduates participated in this experiment in return for course credit. All participants reported having normal or corrected-to-normal vision and were native English speakers. The protocol was approved by the Institutional Review Board of the Johns Hopkins University. All participants provided written informed consent.

Stimuli

The task cues used in the current experiment had two dimensions: color (green/blue) and shape (circle/triangle). During the training phase, participants learned the meaning of the color and shape in two separate sessions. In the color training session, participants responded according to the color dimension of the cue (e.g. green means to perform a phonological task on a presented word and blue means to perform a semantic task on a presented word), and in the shape training session, participants responded according to the shape dimension of the cue (e.g. triangle means to perform a semantic task, and circle means to perform a phonological task on a presented word). The task cue meaning and the rule assignment for both training sessions, as well as the order of the training presented were counterbalanced across participants. The task cues and associated rules are illustrated in Figure 1.

The target word stimuli were nouns with written frequency over 15, taken from the Medical Research Council Psycholinguistic Database (http://websites.psychology.uwa.edu.au/school/MRCDatabase/uwa_mrc.htm). Half of the words had two syllables and the other half had one or three syllables; half had abstract meaning with a concreteness rating below 300 and the other half had concrete meaning with a concreteness rating above 500. Different word stimuli were used in the pre-task training than in the main task.

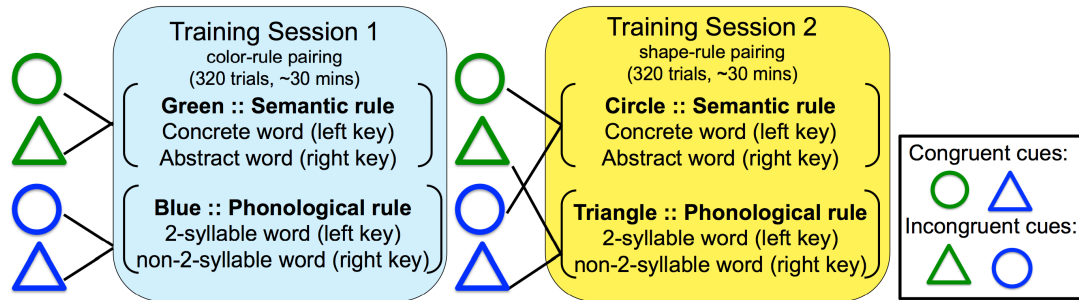


Figure 4.1. Schematic drawing of task cues and their associated task rules.

Each task cue has two dimensions: color and shape. For a given cue, each dimension could either associated with the same task rule (congruent cues) or with different task rules (incongruent cues). During the test phase, the relevant cue dimension remained constant within a block and alternated across blocks.

Procedure

Participants either performed a phonological task or a semantic task for a visually presented word. The phonological task required the participants to indicate by pressing one of two buttons whether the presented word contained two syllables or not. The semantic task required the participants to indicate whether the meaning of the word referred to an abstract concept or a concrete object.

An example trial was illustrated in Figure 4.2. For each trial, the sequence began with a 300-ms task cue indicating the upcoming task, followed by a 300 ms delay. A target word then appeared and remained on screen until a response was made. After each response, feedback was presented for 300 ms to indicate whether the response was “Correct”, “Incorrect” or “Too slow”. The next trial then began after a fixed interval of 3000 ms.

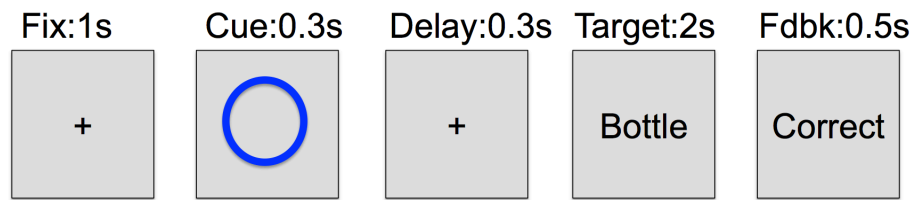


Figure 4.2. Example trial event progression

Participants were instructed to perform tasks according to the relevant cue dimension (color or shape). For each training session, the relevant dimension remained constant throughout the entire session. To ensure both feature dimensions of the cue were *strongly* associated with their corresponding tasks, participants performed 320 trials over a course of 30 minutes on each cue dimension (an hour in total for both the color and shape training sessions) in a quiet laboratory room.

For the test phase, participants performed two experiments, and each experiment consisted of two blocks of 64 trials. In one experiment, the proportion of switch versus repeat trials was manipulated; and in the other experiment, the proportion of incongruent versus congruent trials was manipulated. In each experiment, there were two blocks of 64 trials. One of the blocks had a high proportion of conflict trials and the other one had a low proportion of conflict trials. The order of the experiment and the order of the block presented were counterbalanced across participants. The structure of the study is illustrated in Figure 4.3. For each block, regardless of which conflict type was manipulated, participants were required to attend to the color or shape dimension of the cue

according to a 2-second instruction screen presented every 8 trials (“Attend Color” or “Attend Shape”) throughout the whole block. The relevant dimension alternated across the whole block using a fixed ABAB order.

Proportion conflict manipulation

The proportion conflict manipulation for both types of conflict was done implicitly. Each participant performed two experiments of which one of the conflict types was manipulated.

(1). In the experiment where task-switching was manipulated, the relative proportion of switch versus repeat trials within a block was 75% switch trials and 25% repeat trials for high proportion switch block. Conversely, in the low proportion switch block, the opposite proportion was used (25% switch and 75% repeat trials). In addition, in both the high proportion and low proportion switch blocks, the relative proportion of congruent cue versus incongruent cue trials was kept at 50%.

(2). In the experiment where cue-incongruence was manipulated, the relative proportions of incongruent cue versus congruent cue trials within a block was 75% incongruent and 25% congruent for high proportion incongruence block and opposite proportion was used for the low proportion incongruence block. Also, the relative proportion of switch versus repeat trials for both blocks was kept at 50%. That is, in each experiment, we only manipulated one type of conflict while keeping the other conflict constant.

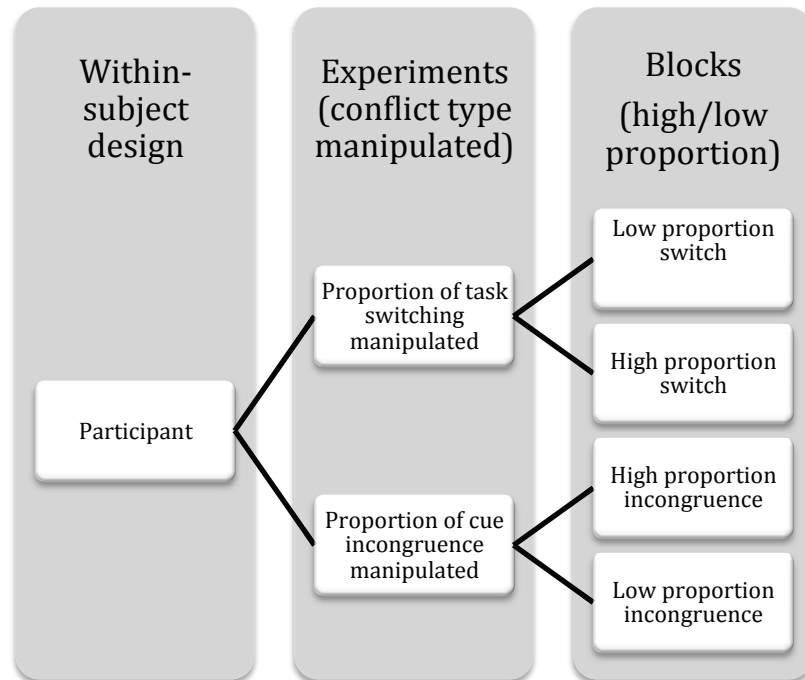


Figure 4.3. An example of the experimental structure. Each participant performed two experiments. In each experiment a different conflict type was manipulated. Each experiment had two blocks of 64 trials in which the proportion of conflict trials was manipulated.

Data Analysis

In order to examine whether the proportion manipulation influenced the costs associated with task switching and cue incongruence, we conducted two independent sets of analyses of variance (ANOVAs), one for each experiment. Each set of ANOVAs had a factorial design of Conflict proportion (high conflict; low conflict) x Cue incongruence (incongruent; congruent) x Task switching (switch; repeat). RT data and error rates data were analyzed separately. Geisser-Greenhouse corrected p values was reported. The first 16 trials of each block were removed, because it is assumed that the control is implemented only

after the participants experienced the level of conflict on the first few trials in a block. The first trial after a change in the color/shape dimension could not be classified as either a switch or repeat trial and so these trials were not included in any of the analyses. Trials with error were also removed. Descriptive statistics are shown in Table 4.1.

4.1.2. Results

In the experiment where the proportion of task-switching was manipulated, the ANOVA on RT revealed a significant main effect of task switching ($F(1,22) = 10.756, p = 0.003$) such that participants were slower in task-switch trials (933 ms) compared to task-repeat trials (882 ms), thus indicating a significant task-switching cost. However, there was no significant interaction between Conflict proportion and Task switching $F(1,22) = 2.437, p = 0.133$, nor between Conflict proportion and Cue incongruence $F(1,22) = 3.208, p = 0.087$, thus indicating that the switching cost was unaffected by the proportion of trials in the block that were switch trials. The proportion of switch trials also did not modulate the size of the effect of the other conflict type, i.e. incongruence costs. These findings are illustrated in Figure 4.4.

For the error rates analysis, the ANOVA revealed marginally significant main effects of task switching ($F(1,22) = 3.607, p = 0.071$) and cue incongruence ($F(1,22) = 4.162, p = 0.054$). There were no significant interactions.

In the experiment where the proportion of cue-incongruence was manipulated, the ANOVA on RT revealed a significant main effect of task switching ($F(1,22) = 20.532, p < 0.001$). However, the main effect of cue incongruence was not significant ($F(1,22) = 1.953, p = 0.176$). This would not be surprising if the size of incongruence costs in the high proportion congruent block were small, rendering the main effect (considering the incongruent effects from both high and low proportion congruent blocks) insignificant. Indeed, we found a significant interaction between block proportion congruence and the congruence of the trial ($F(1,22) = 4.30, p = 0.05$). Therefore, we conducted two post-hoc contrasts, one on high proportion incongruent block, and the other one on low proportion incongruent block. As expected, these follow-up analyses revealed that a significant cue-incongruence effect (incongruent trials = 983 ms; congruent trials = 926 ms) was present when proportion congruent was low ($F(1,22) = 5.021, p = 0.035$), but not (incongruent trials = 943 ms; congruent trials = 946 ms) when the incongruent proportion was high ($F(1,22) = 0.019, p = 0.892$). Finally, there was no significant interaction between the cue congruence proportion and task-switching ($F(1,22) = 0.001, p = 0.978$). Taken together, the significant interaction between block congruence proportion and trial cue-incongruence, and the lack of interaction between block congruence proportion and Task-switching suggest that cue-incongruence effect was susceptible to the proportion congruence manipulation, and this modulatory effect did not transfer to the other conflict type, thus indicating a conflict-specific cognitive control mechanism. The findings are illustrated in Figure 4.5.

For the error rates analysis, the ANOVA revealed significant main effects of cue-incongruence ($F(1,22) = 10.465, p = 0.004$) and proportion congruence ($F(1,22) = 6.79, p = 0.016$). There were no significant interaction effects.

Table 4.1 Descriptive statistics of (A) reaction time data; (B) error rates data.

(A)

	Conflict Manipulated			
	Task switching		Cue incongruence	
	High	Low	High	Low
Switch	0.924	0.942	0.983	0.992
Repeat	0.896	0.869	0.907	0.917
Incongruent	0.922	0.892	0.943	0.983
Congruent	0.897	0.919	0.946	0.926

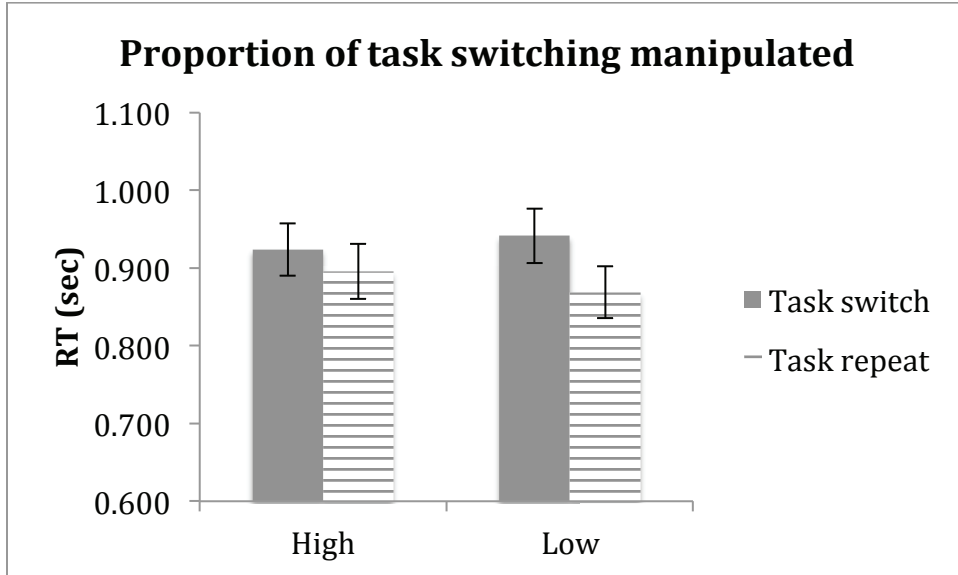
Values are in seconds.

(B)

	Conflict Manipulated			
	Task switching		Cue incongruence	
	High	Low	High	Low
Switch	0.075	0.054	0.082	0.083
Repeat	0.075	0.045	0.040	0.091
Incongruent	0.090	0.063	0.071	0.108
Congruent	0.061	0.035	0.051	0.065

Values are error rates.

(A)



(B)

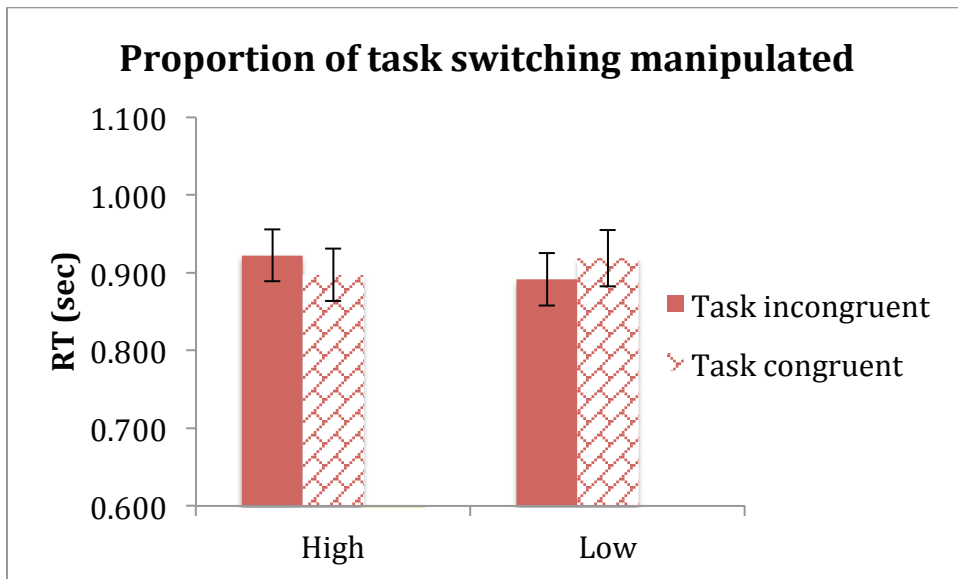
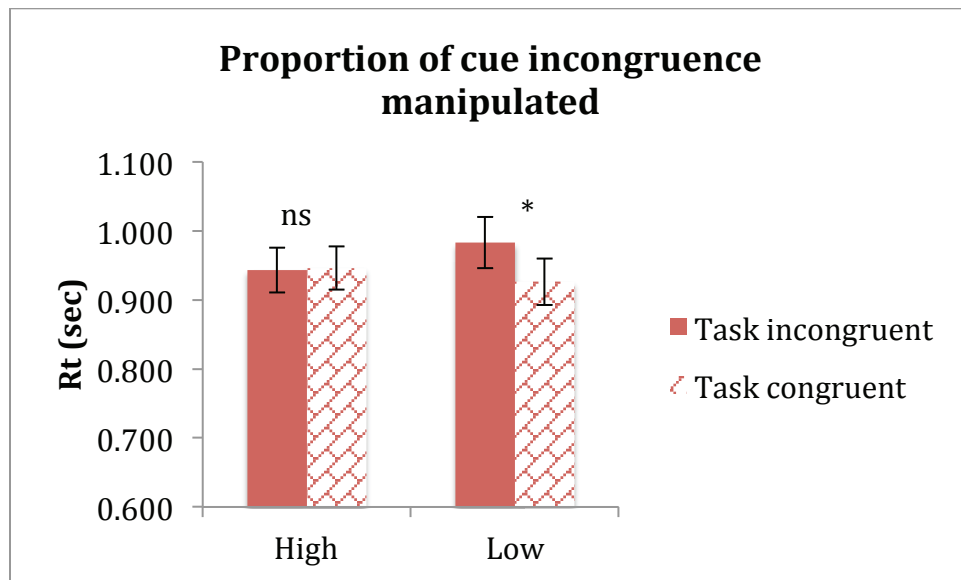


Figure 4.4. The effect of proportion switch manipulation on switch costs and incongruence costs. The low proportion switch block ("Low") indicates 25% switch trials and 75% repeat trials, 50% congruent trials and 50% incongruent trials. The high proportion switch block ("High") indicates 75% switch trials and 25% repeat trials, 50% congruent trials and 50% incongruent trials. Error bars

represent the SEM. (A). Mean reaction time according to the effect of proportion (high/low) on task-switching (task switch/task repeat). (B). Mean reaction time according to the effect of proportion (high/low) on task-incongruence (incongruent/congruent).

(A)



(B)

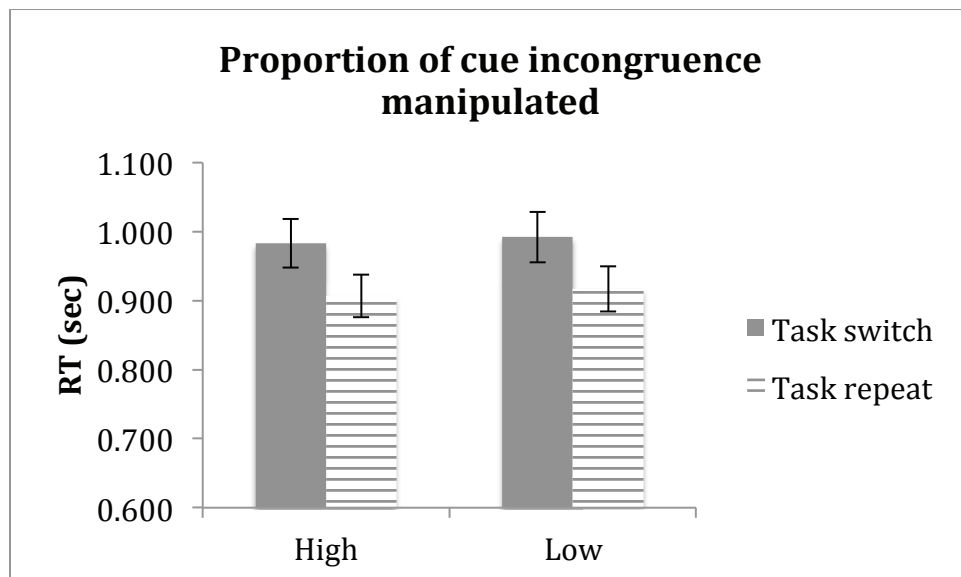


Figure 4.5. The effect of proportion incongruent manipulation on switch costs and incongruence costs. The low proportion congruent condition (“Low”) indicates 25% incongruent trials and 75% congruent trials, 50% switch trials and 50% repeat trials. The high proportion congruent condition (“High”) indicates 75% incongruent trials and 25% congruent trials, 50% switch trials and 50% repeat trials. Error bars represent SEM. (A). Mean reaction time according to the proportion congruent (high/low) and trial congruency. (B). Mean reaction time according to proportion congruent (high/low) and whether the trial was a task switch or a repeat. The asterisk denotes statistical significance ($p < 0.05$) for the post-hoc contrasts.

4.1.3. Discussion

The current experiment is, to our knowledge, the first to demonstrate dissociable effects of a cognitive control modulation on different types of task conflict, namely the task-switching conflict and cue-incongruence conflict. One novelty of the current experiment was the use of a new paradigm that directly introduces different degrees of conflict at the task level, independent of particular stimuli or specific motor responses involved in the task. We found proportion-conflict effects could be observed in the situation where the proportion of cue incongruence was manipulated. Higher proportion of incongruent trials resulted in a smaller incongruence cost, as compared to low proportion of incongruent trials. In addition, the proportion congruent effects did not transfer to the other

conflict type. That is, the task switch costs remains virtually the same regardless the proportions of incongruent trials within a block. The pattern of results provides evidence for a conflict-specific account of cognitive control with respect to cue-incongruence conflict. In addition, task-switching costs were also unaffected by the proportion of switch trials in a block. The fact that task-switching conflict resolution and cue-incongruence conflict resolution were modulated differently by the proportion manipulation suggests a distinction between them. It appears that both types of conflict caused interference to the cognitive system, as evident by high conflict trial types (i.e. task-switching trial and task-incongruent trials) being associated with significant costs in terms of task performance. However, only cue-incongruence conflict appeared to be modulated by a proactive conflict monitoring system. Taken together, our conclusion is consistent with the idea that there are distinct cognitive control mechanisms for resolving different types of task conflict, namely the switching-induced and incongruence-induced task conflict, because they respond differently to the proportion manipulation. The cognitive control mechanism for resolving cue-incongruence appears to be conflict-specific, such that resolution of cue-incongruence conflict did not result in facilitation or impairment of conflict resolution for task-switching conflict.

At the first glance, the finding that task-switching costs were unaffected by the proportion congruence effects seems at odds with previous literature, which showed task-switch costs are larger for high proportion task-repeat than for low proportion of task-repeat blocks of trials (e.g. Dreisbach et al., 2002; Dreisbach

and Haider, 2006; Schneider and Logan, 2006). However, one can speculate that the discrepancy of results might be explained by the task paradigm that we used. Specifically, these studies aforementioned used a task-switching paradigm in which the tasks involve either performing parity or magnitude judgments on digits (1 to 9, except 5). One recurring issue with this paradigm is that task conflict, which by definition is caused by frequent changes of task identity, is often confounded with response conflict, which occurs when the correct response for a given target is either different (incongruent response) or the same (congruent response) according to the task rule. On the other hand, in our paradigm, we use trial-unique targets (i.e. each word was only used once in the entire experiment), thus obviating the possibility of participants forming associations between the target words and a response. In fact, in a separate analysis, we found no significant difference in reaction time between the response-congruent trials and response-incongruent trials (analysis is not shown here). Therefore, it is likely that in the previous studies, the proportion switching effects are indirectly modulating the task-switch costs through reducing response conflict on repeat trials rather than by facilitating task-switching.

One question raised by the current study is how conflict proportion within a block influences the cost associated with resolving cue-incongruence conflict. According to the early accounts, proportion congruent effects can be explained by the adoption of a sustained or proactive control strategy or task set, which prepares the attentional system to handle interference from the upcoming distracting feature of the incongruent cue. For example, Logan and Zbrodoff

(1979) proposed that participants develop expectancies about the proportion of conflict trials and voluntarily shift their attentional strategy according to the conflict levels. That is, when the proportion of incongruent trials is low, participants detect that conflict is infrequent and thus allow their attention to be drawn to the more salient information, because the salient information frequently corresponds to the correct response. Such strategy would speed up processing of congruent trials (the task-irrelevant information has a facilitating effect), and slow down processing of incongruent trials (more interference from the irrelevant dimension). On the other hand, when the proportion of incongruent trials is high, the best strategy is to inhibit attention to the irrelevant information. Such strategy would slow down processing of congruent trials (lack of a facilitating effect) and speed up incongruent trials (better attentional filtering of the irrelevant information), and thus generate smaller interference effects. In relation to our experiment, proportion congruent manipulations may influence how strongly contextual information is maintained. In our task, the cues that indicate the upcoming task had a relevant and an irrelevant dimension, and they could either indicate the same task rule (congruent trial) or different task rules (incongruent trial). Since the relevant dimension alternated within a block (every 8 trials in a block of 64 trials), participants were required to maintain the currently relevant context (“attend color” or “attend shape”) in working memory. Thus, when the proportion of incongruent trials was low (mostly congruent trials), participants may have resorted to a reflexive or stimulus/cue-driven control strategy, because the congruent cues were usually associated with the same task, regardless of the

current context (“attend color” or “attend shape”). When an infrequent incongruent cue appeared, participants were less prepared to select the relevant dimension of the cue; hence the lengthened reaction time for the incongruent trials and greater incongruence costs. On the other hand, when the proportion of incongruent trials was high (mostly incongruent trials), participants may have adopted a strategy of maintaining a strong and sustained representation of the currently relevant context. Therefore, the reaction time for processing incongruent cues is reduced due to better attentional focus on the relevant dimension of the cue, whereas the reaction time for processing congruent cues is lengthened because there is less of a facilitating effect from the irrelevant but congruent information.

In conclusion, the current study extends the existing literature by showing that proportion of high or low conflict trials that are in a block can affect conflict resolution involving abstract task rules, independently from stimulus-stimulus conflict or stimulus-response conflict. Furthermore, our data also suggests there are distinct cognitive control mechanisms for resolving different types of task conflict, namely the switching-induced and incongruence-induced task conflict, because they respond differently to the proportion manipulation. Finally, the cognitive control system for resolving cue-incongruence conflict operates in a conflict-specific manner, supporting the conflict-specific account of cognitive control. These results not only show evidence supporting distinct cognitive control mechanisms for resolving different task conflict types, but also challenge the conflict-monitoring theory, which claims that the conflict-control loop is only

sensitive to the general level of conflict within the system, regardless of the source of the conflict (Botvinick et al., 2001)

5. Chapter 5: General Conclusions

5.1. Findings of this dissertation

Establishing how abstract rule-like information is controlled and selected for further processing is essential to our understanding of higher cognitive functions. This dissertation sought to investigate the conflict-driven cognitive control mechanisms in humans for resolving conflict among abstract representations of non-sensory information. The overarching aim was addressed using neuroimaging techniques and behavioral manipulations. The first study investigated the cognitive control mechanisms for resolving conflict among abstract rules. The second study sought to examine whether different types of rule-related conflict, namely task-switching and cue-incongruence, recruited similar or dissociable neural systems. Finally, the third study investigated whether qualitatively distinct cognitive control mechanisms were involved in resolving conflict associated with task-switching and cue-incongruence.

In Chapter II (Experiment 1), the primary goal was to test whether the cognitive control mechanisms involved in resolving conflict among abstract representations were similar to those involved in resolving sensory representations. A new paradigm was developed in which participants were trained to associate the color and shape dimensions of the cue with either the same rule (congruent cues) or different ones (incongruent cues). This enabled us to manipulate the degree of conflict at the task-rule level, independently of the sensory features of the task cues or any motor responses triggered by the

targets that the rule applied to. In addition, semantic and phonological tasks were chosen because (1) they are abstract rules that are not tied to specific stimulus-response associations or any sensory features; and (2) previous studies have shown that they preferentially activate distinctive brain regions. These properties allow us to use the activity in these task-selective areas as a proxy for measuring the degree to which the conflict between relevant versus irrelevant rule representations was resolved. This study demonstrated that incongruent cues are associated with a greater behavioral cost compared to congruent cues, and this behavioral effect was accompanied by increased activity in several brain areas, including inferior frontal gyrus, inferior parietal lobule, subcortical areas, and insula. Importantly, the conflict between abstract representations of task rules was resolved by feedback from the right inferior frontal gyrus (rIFG) enhancing the activity of the brain region processing the relevant abstract information, rather than suppressing the activity of the brain region processing the irrelevant abstract information. Multivoxel pattern classification analysis further revealed the representational content within the rIFG contains both contextual and rule information, suggesting rIFG biases selection of the appropriate abstract task representations according to both the cue and the more temporally extended context.

In Chapter 3 (Experiment 2), the same data set from Experiment 1 was used to answer a different research question. The goal is to examine the generality of cognitive control for abstract representations by asking whether different sources of conflict pertaining to task rules recruited a single cognitive

control neural system or dissociable cognitive control neural systems. Cued task-switching and incongruence tasks are two commonly used paradigms to study the mechanisms of cognitive control concerning task rules. Despite the presence of conflict between a relevant and an irrelevant task rule in both paradigms, the sources of conflict originate differently. In this experiment, we take advantage of the task design in Experiment 1, in which the task-switching conflict and cue-incongruence conflict were factorially combined, to answer the generality question of cognitive control. The fMRI results from this study show that switching-induced and incongruency-induced conflict recruit distinct brain networks, which indicates that independent conflict-driven cognitive control loops are involved to resolve different types of task-rule conflict. Findings also suggest that task switching and cue incongruence activate left-lateralized and right-lateralized frontoparietal networks, respectively. This lateralization may reflect different cognitive control processes needed for successfully resolving incongruency-induced and switching-induced conflict, as previous studies have shown that a sustained, block-wise, cognitive control component activates right-lateralized frontoparietal brain regions, while a transient, trial-by-trial, cognitive control component activates left-lateralized frontoparietal brain areas. This offers further evidence that task-switching and cue-incongruence are processed as different types of conflict and may require qualitatively different control modes to resolve each of them independently.

Finally, in Chapter 4 (Experiment 3), we continued the same line of research as in Chapter 3 (Experiment 2) and asked whether the conflict-driven

cognitive control mechanisms responsible for resolving task-switching and cue-incongruence conflict are similar or qualitatively different. This was investigated by employing a behavioral proportion manipulation (changing the frequency of conflict trials within a single block). We found proportion conflict effect (greater behavioral cost for low proportion of conflict trials compared to high proportion of conflict trials) only when the ratio of incongruent cue versus congruent cues was manipulated, but not when the ratio of switch versus repeat trials was manipulated. In addition, regardless of which type of the conflict was manipulated, control recruited by one type of conflict did not result in resolution of the other type. Thus, the fact that the same proportion-of-conflict manipulation produces different conflict resolution effects suggests qualitatively distinct cognitive control mechanisms are at work in order to resolve these two types of rule-related conflict.

Taken together, by using a novel paradigm that directly manipulates the degree of conflict at the task-rule level, our studies provide better understanding of the mechanism by which conflict among abstract representations of rule information may be resolved. This conflict-driven control mechanism resolves conflict among abstract representations of task rules by selectively enhancing activity in areas processing the relevant abstract information (Experiment 1). This is in agreement with previous selective attention studies that showed competing sensory stimuli were resolved through enhancement of brain area coding the relevant sensory information (e.g. Egner and Hirsch, 2005). In addition, the conflict-driven control mechanisms for task rules operate in a

conflict-specific manner. Rather than monitoring the general level of conflict in the system, the conflict-driven cognitive control mechanisms are sensitive to the source of these rule conflicts and how they are generated (Experiment 2-3). Overall, our studies provided invaluable insight regarding the cognitive control mechanisms for abstract rule information. Given that many higher cognitive functions, such as planning, reasoning, problem solving, highly rely on the ability to represent and select appropriate rules, our studies made it more tractable to understand how these higher cognitive functions are achieved. In the section that follows, I consider the theoretical implications of our findings, with reference to Miller and Cohen's Integrative Theory of Cognitive Control (Section 5.2), followed by open questions generated by the current dissertation (Section 5.3), and a final reflection on the findings of this dissertation (Section 5.4).

5.2. Examining the Implications for Theory of Cognitive Control

Miller and Cohen (2001) integrative theory of PFC function is one of the most influential models of cognitive control. The model states that the prefrontal cortex (PFC) exerts control over other brain areas by representing and maintaining goals or task rule information. Specifically, the rule representations in the PFC are like "maps", which configure the neural pathways within and between other brain areas that are needed to perform the task. They draw explicitly upon Desimone and Duncan (1995) biased competition theory of visual attention, in which attention was conceptualized as a biasing signal that

modulates the mutually inhibitory interactions among populations of neurons. The increased activity of neurons representing the attended stimulus, by virtue of mutual inhibition, results in the suppression of other neurons representing the irrelevant stimuli. According to Miller and Cohen, this mechanism of biased competition not only occurs between the PFC and visual cortex, but also with other sensory modalities, as well as systems responsible for movement execution, memory retrieval, and emotion evaluation. Therefore, they proposed that biased competition serves as a fundamental mechanism by which PFC exerts control over other brain systems to produce goal-directed behavior.

While Miller and Cohen proposed that the PFC biases neural processing in the rest of the brain by representing and maintaining a particular type of information: the rules of a task, it is unclear whether such process of biased competition also occurs within the PFC itself when there is a competition between abstract representations of task rules. In Section 1.3.1, I reviewed human neuroimaging and monkey neurophysiological studies that showed populations of neurons in PFC can represent abstract rule information that is independent from the sensory properties of the cue and anticipated motor responses. However, none of the previous studies have examined the cognitive control mechanisms for selecting the relevant rule over the irrelevant ones to guide behavior, particularly when the task demands are frequently changing which places greater emphasis on the control process to select the appropriate rule to meet the current task demand. Experiment 1 addressed this question by showing that when there is a competition between abstract rules, the conflict was

resolved by right inferior frontal gyrus providing the bias signals to select the relevant rule information, rather than suppressing the irrelevant rule information. Such pattern of results were exemplified by the greater rIFG involvement during the incongruent trials predicts the greater enhancement of activity in the brain areas processing the relevant abstract information associated with the task rule. Therefore, our findings have important implications for Miller and Cohen's cognitive control theory, suggesting that abstract rule information should be treated as a type of information, which is itself subjected to the principles of biased competition.

Our results are also different from what the biased competition model would predict in the sense that we did not find any direct competition or inhibition of the irrelevant abstract information. It is important to note, however, that the inhibition is a result of selective attention via the local mutually inhibitory interactions within the receptive fields of the same neurons. Such inhibitory mechanism may be difficult to observe between separate cortical areas because they are not likely to share strong inhibitory connections with each other. Thus, the enhancement of neural activity in one area would not necessarily be expected to result in inhibition of the other. Furthermore, previous studies have highlighted the difficulties in using fMRI to investigate inhibition in posterior cortical regions (for a review, see Aron, 2007). One problem is the fMRI signals may not capture the neural inhibition effect despite another method can clearly demonstrate GABA-mediated neural inhibition (Waldvogel et al., 2000). Another problem is that the definition of inhibition using fMRI measure is the relative

difference between task condition and baseline. Therefore, if the baseline activity in an area has higher activity during rest, then the contrast would show up as deactivation, which makes it difficult to interpret such result as inhibition at the neural level (Stark and Squire, 2001).

Overall, we extended the notion of biased competition, at least in the case of enhancing relevant information, to processes within the PFC and proposed that PFC is the source of the bias signals representing task rules as well as the target of that signals when competition between task rules occurs.

5.3. Open Questions

The work presented in this dissertation provides new insights regarding how conflict-driven cognitive control mechanism resolves conflict among abstract representations of rule information. These findings also open up a rich set of questions for future investigation on how other domains of cognitive control are implemented when the information involves abstract rules.

Conflict Resolution versus Integration

PFC has been implicated in other control processes that appear to extend beyond simply resolving conflict between competing representations. For example, PFC has shown to be sensitive to conditions that require subgoal and/or integration across representations (Koechlin et al., 1999). Braver and

Bongiolatti (2002) used fMRI to test whether the frontopolar region of prefrontal cortex is involved in integration of two sources of information for target determination. They asked participants to monitor for the presence of any concrete probe word immediately following any abstract cue word, which would require the participants to first perform a semantic classification and then relate the subsequent categorization result to the semantic status of the next word in sequence (i.e., participants required to integrate two sources of information to make a correct response). The results demonstrated that lateral frontopolar cortex subserves higher-order control processes such as subgoaling and integration. Thus, another important question to address here is how other cognitive control processes, such as subgoaling/integration, are implemented when the information involves abstract rules. Experiment 1 showed that when there is a conflict between task rules, the conflict was resolved by right inferior frontal gyrus enhancing the relevant abstract representation pertaining to the relevant task rule. Since integration/subgoaling and conflict resolution are two very different cognitive control processes, their underlying neural mechanisms may be qualitatively different from each other. It will be interesting to test how prefrontal cortex interacts with task-selective areas when the task demand requires integration of task rules, rather than selection of the relevant task rule over the irrelevant ones. Studying how other cognitive control processes are implemented when the information involves abstract rule representations would help us better understand how other higher-order cognitive functions such as planning, problem solving and reasoning are achieved.

Enhancement versus suppression

Top-down cognitive control can be achieved by enhancing the relevant information, suppressing the irrelevant information, or both (Cohen et al., 1990). Experiment 1 demonstrated that conflict resolution between task rules was resolved by right inferior frontal gyrus (rIFG) selectively enhancing the brain area processing the relevant abstract information pertaining to the relevant rule, rather than by suppressing the brain area processing the irrelevant abstract information pertaining to the irrelevant rule. However, suppression of irrelevant task information may still be a plausible mechanism that solves conflict between task rules when the task demand favors suppression. For example, a study by Yeung and colleagues (2006) investigated the cognitive control mechanism of between-task competition using task switching paradigm. On each trial, they showed participants overlapping face and word stimuli, and the participants were required to either classify the gender of the face (face task) or the word as having two syllables or not (word task), depending on a task cue presented at the beginning of each miniblock. Across miniblocks, the participants either had to switch to a different task or repeat the same task. They found that regions selective for the irrelevant task showed increased activity during switch and that the switch costs correlated with the activity in the task-irrelevant area, rather than the activity in the task-relevant area. The observed pattern of results suggests that

interference from recently performed task significantly contributes to the behavioral switching costs.

In Experiment 1 and 2, to solve the cue incongruence, it requires active maintenance of contextual information (shape or color) to proactively prevent the activation of irrelevant rule representations. In contrast, when little time is available for preparation as in the case of task switching, the cognitive control mechanisms may operate differently. Experiment 2 and 3 have shown that conflicts arising from task-switching and cue-incongruence recruit anatomically distinct neural circuits and that their underlying cognitive control mechanisms are qualitatively different. Thus, it would be interesting to use the current paradigm to investigate how PFC interacts with task-selective areas during task switching. Based on Yeung et al.'s result (2006), one hypothesis would be that PFC resolves task-switching conflict by suppressing the activity in the task-irrelevant area. Future research would need to confirm that.

Cognitive flexibility and cognitive stability

Experiments 2 and 3 showed that conflict induced by task-switching and cue-incongruence were resolved by qualitatively different cognitive control mechanisms and they recruited anatomically distinct neural circuits. Particularly, when correlating switch costs with incongruence costs across individuals, there is no correlation between the two. Upon reflection, the best strategy to resolve cue-incongruence conflict was to maintain a clear and focused representation of the

current contextual information (“Attend Color” or “Attend Shape”) in working memory to guide the selection of the relevant task rule associated with the context in effect. On the contrary, the best strategy to resolve task-switching conflict was to flexibly and quickly switch to the currently relevant task rule and disengage the irrelevant one, on a trial-by-trial basis. Thus, despite the task requirements being the same: selecting the relevant task rule over the irrelevant one, the exact cognitive control requirements are different: one requires cognitive stability (i.e. our ability to adhere to behavioral goals in the face of interference) and the other one requires cognitive flexibility (i.e. our ability to flexibly adjust behavior according to the change of environmental demands).

Using fMRI in healthy humans, Armbruster et al. (2012) showed individual differences among participants such that those who spontaneously switch more frequently are more distractible as measured by the number of errors they make in the presence of a distractor. Moreover, more flexible persons (those who are more ready to switch spontaneously under the ambiguous condition) activated the left-lateralized task-switching areas (inferior frontal junction [IFJ], basal ganglia) less than inflexible people during task switching. Most importantly, the functional coupling between IFJ and superior frontal gyrus (SFG) is task dependent: their activities were positively correlated with the spontaneous switching rate during distractor inhibition and negatively correlated with the spontaneous switching rate during task switching. Thus, high connectivity between these two areas appears to be necessary for suppressing the

distractors and decreased connectivity appears to be necessary for successful task switching.

It will be interesting to relate the current findings (i.e. no correlation between switch costs and incongruence costs across participants) to individual differences in cognitive flexibility and cognitive stability. By examining whether switch costs and incongruence costs associated with differences in activation or functional connectivity between brain areas, we can explore the individual differences in cognitive flexibility versus stability and its underlying neural basis.

5.4. Final reflection

This dissertation was conceived upon the observation that previous theories of conflict-driven cognitive control have been largely focused on the control over perceptual representations of stimuli that are transiently present in our environment or control over motor responses. There are a few studies that have examined how selection of abstract conceptual representations is accomplished by manipulating competition between lexical representations during word production (Robinson et al., 1998) between phonological representations using a stem completion task (Desmond et al., 1998), or between semantic representations using semantic priming paradigm (Metzler, 2001). The competition between abstract rule representations has not been fully examined, however, until now. When I began graduate studies, a group of researchers had demonstrated that rules could be actively maintained as a type of information in

working memory to guide behavior, and that prefrontal cortex neurons can encode/represent abstract rule information. In our daily lives, we use a variety of abstract rules (e.g. social rules) and constantly shift them to meet the environmental demands. That initiated my interest in examining the control mechanisms that govern abstract rule information.

Most studies on the cognitive control of task rules employ a task-switching paradigm or an incongruence paradigm. However, one issue that became increasingly problematic was that it was difficult to dissociate rule representations from the sensory cue that signifies the rule or the anticipated response association that was tied to the stimulus. Therefore, I began my challenging task of designing a parsimonious paradigm that could independently manipulate the degree of conflict directly at the task-rule level. Moreover, the special choice of semantic and phonological tasks allows me to measure how much of the competition between the relevant and the irrelevant rule was resolved.

Taken together, the studies that I presented in this dissertation demonstrated a mechanistic view of how conflict among abstract rule representations is resolved and offered a conflict-specific account of the cognitive control mechanism for dealing with different sources of rule conflict. These results extend Miller and Cohen's (2001) cognitive control model by suggesting a similar biased-competition-like process that occurs between PFC and posterior areas also occurs within the PFC itself. The process is somewhat different, however, in that the selection of relevant rule over the irrelevant ones is achieved solely by enhancing the relevant rule representation, which is reflected by the

correlation between rIFG activity and the degree to which the task-relevant information is enhanced, and not by inhibiting the irrelevant information. By studying the cognitive control mechanism of task rules in various cognitive domains (conflict resolution, integration, inhibition), understanding of higher-ordered functions such as planning, reasoning, and problem-solving may become more tractable.

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Curriculum Vitae

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EDUCATION

The Johns Hopkins University, Baltimore, MD
Ph.D., Psychological and Brain Sciences 2015
Dissertation: "Cognitive Control of Abstract Rules" (Advisor: Dr. Susan Courtney)

The Johns Hopkins University, Baltimore, MD
M.A., Psychological and Brain Sciences 2011
Thesis: "Neuroplasticity Underlying Working Memory Networks: Evidence From ICA-Based fMRI Analysis in Patients with Multiple Sclerosis"

National Taiwan University, Taipei, Taiwan
B.S., Psychology (Graduated on Dean's List) 2006

AWARDS AND HONORS

Taiwan Ministry of Education Advanced Study Scholarship 2009 – 2011
Two years of tuition and life expenses support for a total of \$50,000 USD.

WORKING EXPERIENCE

McLean Hospital/Harvard Medical School, Belmont, MA
Developmental Biopsychiatry Research Program, P.I. Martin Teicher, M.D., Ph.D.

Research Specialist March 2008 – April 2009

Conducted sophisticated statistical analysis on neuroimaging and behavioral data, which resulted in numerous peer-review publications in high impact journals. Directly involved in the writing, reviewing, and editing of scientific manuscripts. Performed literature review for grant proposals. Presented research in scientific conferences. Assisted grant proposal submission and annually

progress report for several federal funded research projects.

Research Assistant

June, 2006 – Feb.2008

Managed and maintained a database over 250 human brain imaging data and psychological testing data. Coordinated research studies and recruitment. Assisted federal grant proposal submission, including pilot data collection and analysis. Presented research in scientific conferences.

TEACHING EXPERIENCE

Teaching Assistant, Department of Psychological and Brain Sciences, Johns Hopkins University

Undergraduate

Law, Psychology, and Policy-making	Fall, 2014
Research Methods in Experimental Psychology	Spring, 2012
Physiological Psychology	Fall, 2010
Functional Human Neuroanatomy	Spring, 2010

Graduate

Advanced Statistical Method	Fall, 2011
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Guest lecturer

Cognitive Control	Fall, 2011
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PEER-REVIEWED PUBLICATIONS

- Tomoda A, Suzuki H, Rabi K, **Sheu YS**, Polcari A, Teicher MH (2009) Reduced prefrontal cortical gray matter volume in young adults exposed to harsh corporal punishment. *Neuroimage* 47 Suppl 2:T66-71.
- Sheu YS**, Polcari A, Anderson CM, Teicher MH (2010) Harsh corporal punishment is associated with increased T2 relaxation time in dopamine-rich regions. *Neuroimage* 53:412-419.
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- Tomoda A, **Sheu YS**, Rabi K, Suzuki H, Navalta CP, Polcari A, Teicher MH (2011) Exposure to parental verbal abuse is associated with increased gray matter volume in superior temporal gyrus. *Neuroimage* 54 Suppl 1:S280-286.

Walsh M, Montojo CA, **Sheu YS**, Marchette SA, Harrison DM, Newsome SD, Zhou F, Shelton AL, Courtney SM (2011) Object working memory performance depends on microstructure of the frontal-occipital fasciculus. *Brain connectivity* 1:317-329.

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- Seraphin, S. B., Teicher, M. H., Rabi, K., **Sheu, Y. S.**, Andersen, S. L., Anderson, C. M., Choi, J., Tomoda, A. (2010). Ontogenetic perspectives on the neurobiological basis of psychopathology following abuse and neglect. In Worthman, C. M., Plotsky, P. M., Schechter, D. S., Cummings, C. A. (Eds.) *Formative Experiences* (p.p. 308-330). New York: Cambridge University Press
- Teicher, M. H., Rabi, K., **Sheu, Y. S.**, Seraphin, S. B., Andersen, S. L., Anderson, C. M., Choi, J., Tomoda, A. (2010). Neurobiology of childhood trauma and adversity. In Lanius, R. A., Vermetten, E., Pain, C. (Eds.) *The Impact of Early Life Trauma on Health and Disease* (p.p. 112-122). New York: Cambridge University Press

PUBLISHED ABSTRACTS AND CONFERENCE PROCEEDINGS

- Sheu, Y. S.** & Courtney, S. M. (2014). A conflict-specific cognitive control mechanism for task rules: switching between task rules and resolving rule conflicts. *Proceedings of society for neuroscience, the 44th Annual Meeting* (Washington DC, USA)
- Sheu, Y. S.** & Courtney, S. M. (2013). Testing the biased competition model of attention in the selection of abstract task rules. *Proceedings of society for neuroscience, the 43th Annual Meeting* (San Diego, USA)
- Sheu, Y. S.**, Montojo, C., Walsh, M, Courtney, S. M. (2010). Altered prefrontal connectivity during spatial and object working memory performance in multiple sclerosis. *Proceedings of the cognitive neuroscience society (CNS), Annual Meeting*. (Montreal, Canada)
- Sheu, Y. S.**, Polcari, A., Teicher, M. H. (2008). The effect of methylphenidate on functional connectivity of the default mode network. *Proceedings of society for neuroscience (SfN), the 38th Annual Meeting*. (Washington DC, USA)

LANGUAGES

- Mandarin – native language
English – speak fluently and read/write with high proficiency

MEMBERSHIPS

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